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ARCHIVES OF DISEASE IN CHILDHOOD

INCORPORATING THE BRITISH JOURNAL OF CHILDREN'S DISEASES

CONTENTS

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ARCHIVES OF DISEASE IN CHILDHOOD

EDITORIAL STATEMENT

With its 101st number the Archives enters upon a new phase, for it now incorporates THE BRITISH JOURNAL OF CHILDREN'S DISEASES. It is therefore a suitable moment to record the brief history of these two journals and to take a glimpse at the future. The B.J.C.D. made its first appearance in 1904 under the editorship of the late Dr. George Carpenter, who, in an editorial note, observed that in the British Isles there was then no periodical which dealt with disease in childhood, although America, France, Germany and Italy were making headway in this special field of medical literature. In 1900 the Society for the Study of Disease in Children had been founded, and undoubtedly its growing strength hastened the birth of a special journal. Carpenter was much helped in his enterprise by the late Mr. R. E. Adlard, of the printing firm of Adlard and Son, Ltd. Dr. Carpenter had saved the life of one of the children of Mr. Adlard, who showed his thankfulness by launching and financing the BRITISH JOURNAL OF CHILDREN'S DISEASES, now no longer published as a separate journal.

THE ARCHIVES OF DISEASE IN CHILDHOOD first appeared in 1926, largely through the energies of the late Dr. Hugh Thursfield and the late Sir Dawson Williams, then editor of the BRITISH MEDICAL JOURNAL, who retained a life-long interest in diseases of children. The new journal was welcomed in an article in the B.M.J. in these terms:—

'Nearly a year ago some of the medical men whose work lies chiefly among children, and who for a considerable time had felt that English work in this branch of medicine was inadequately presented by existing publications, met together and, after discussion, determined to sound their colleagues on the advisability of establishing a new journal.'

The Editors of the Archives have striven to maintain a high literary and scientific standard, and the current issue, the first run of the second hundred, sees it strengthened by its absorption of another journal, and the formal recognition of the strong link that has always existed between it and the British Paediatric Association. The appointing of Editors and Editorial Committee and Board is now a joint function of the B.M.A. and the B.P.A. The British Paediatric Association has, in recent times, shown its active concern with the preventive aspects of child health, and, no doubt, this will be reflected in the editorial policy of the Archives, which should therefore have a wider appeal in the future, especially to those practitioners whose work among children is associated with that of local health and education authorities.

Much of the preventive medicine of childhood must rest upon the scientific study of disease. The recognition of the disease rickets, for example, and the discovery of its cause have made it possible to plan preventive measures in a scientific way; and so with scurvy. Protective inoculation against such infections as diphtheria, the diagnosis of foot faults and faults of posture, the study of the abnormal behaviour of the 'problem child'—all these are witness to the fact that the approach to health has often to be made by a study of abnormal. The standards of the normal, of 'positive health,' are but little known, so the title of the ARCHIVES, if it does not reflect the new optimism, at least reflects what is and not what might be.

A CENTURY OF CHANGES IN THE MORTALITY AND INCIDENCE OF THE PRINCIPAL INFECTIONS OF CHILDHOOD

BY

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(Medical Officer, Ministry of Education)

This article is based on the Milroy lectures delivered before the Royal College of Physicians of London in 1944, but some of the introductory matter has been omitted and modifications and additions have been made. Its object is to give a general account of the behaviour of the chief killing diseases of children from the establishment of universal registration in July, 1837, to the present time. It is inevitably much more a study of mortality than of incidence because the information about mortality is so much more complete and goes back so much further than does that about incidence.

In his review of a hundred years of death registration the Registrar-General (Text, 1937) gave a table which showed that in the first year of civil registration, from July 1, 1837 to June 30, 1838, there were 156,817 deaths in England and Wales among children under 15 years of age. By applying the death-rates in different age groups in 1937 to the estimated population by sex and age at the end of 1837 he then calculated the number of deaths which would have occurred if the rates of 1937 had prevailed in 1837. The figure was 38,719—slightly less than a quarter of the actual number of deaths registered. These figures are for deaths from all causes and include deaths from conditions peculiar to infancy and from violence which have not decreased to anything like the same extent as have those due to infections. The reduction in mortality from infections has therefore been even more remarkable than these figures suggest.

It may, at first sight, seem to be a hopeless task to give any useful picture of the history of mortality from individual infections in childhood because of their variety and because of ' the eternal difficulty of comparability between diagnosed causes of death at different epochs ' (Greenwood, 1935). Though children die from many different causes the number of diseases which kill large numbers is comparatively small and most of them were well separated a hundred years ago—long before the birth of bacteriological methods of diagnosis. There are important exceptions to this last statement for deaths from scarlet fever and diphtheria were not shown separately by the Registrar-General until 1858, and those from typhus and typhoid were not separated until 1869. This does not mean that before 1869 clinicians were incapable of distinguishing a case of typhus from a case of typhoid but only that they ' were less alive to the general hygienic implications of the separation than we are ' (Greenwood, 1935). There is an added difficulty about the early statistics of diphtheria in that many cases of diphtheria were thought to be due to a separate disease—' croup '—but not all cases of ' croup ' were diphtheria.

In considering the trends of death-rates from separate causes there are advantages in beginning rather later than 1837 because the information available in later years is so much more complete. The next great landmarks in the history of vital statistics after the establishment of civil registration are two Supplements to the Registrar-General's Annual Reports, the first being the Supplement to the 25th Annual Report covering the ten years 1851–60 and the second the Supplement to the 35th Annual Report covering the years 1861–70. These two reports, particularly the second, may be described as the principal foundation of this paper. The Supplement to the 35th Annual Report is much more than a mere review of the ten years immediately preceding and it has been described as the ' crowning effort of Dr. Farr's labour at the General-Register Office ' (Farr, 1885).

In preparing a survey of so wide a field the temptation to stray down interesting side tracks is considerable and so it seems desirable to set out certain fundamental questions to give direction to the whole study.

(1) How many children have there been in England and Wales at different times?

(2) How many have died?

(3) Of what diseases did they die?

(4) How many have suffered from those diseases for which records of incidence are available?

(5) How much information about the causes of high mortality and sickness rates in childhood can be gained from a study of their variations in time and among different sections of the population?

The first two questions are easy to answer

reasonably accurately, but there is some inaccuracy in that, prior to the Notification Act of 1874, the notifications understated the number of births because the previous Act did not impose any penalty for failure to register. The census returns for ages 0–5 were unreliable and even in the last census of 1931 the numbers of young children differ from the totals expected from births and deaths. The third is less easy because of the great changes in medical knowledge over so long a period. The fourth is still more difficult because it depends on notification returns and the answer to the fifth question must consist in large measure of speculation.

The answer to question 1 is given in fig. 1 which

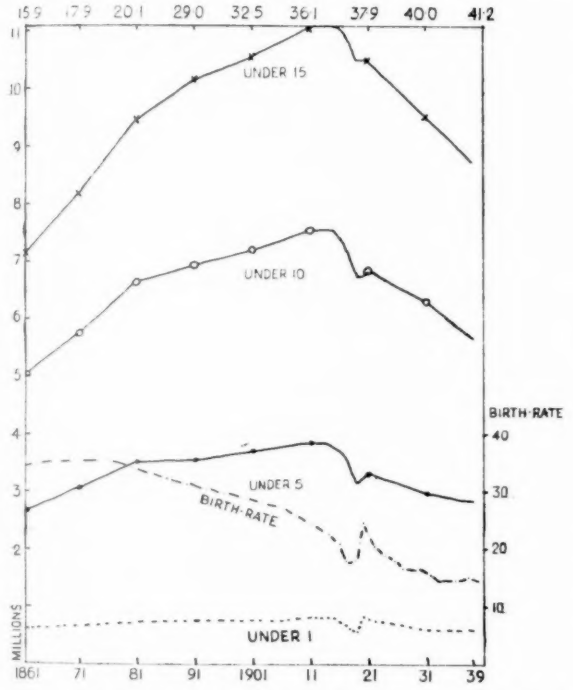

FIG. 1.—England and Wales: Populations 1861–1939. Total (millions).

shows the number of children living in different age groups at the decennial censuses since 1861. It includes also a curve of the changes in the birth-rate and details of the changes in child population in the last war based on the estimates of population given in the Registrar-General's Decennial Supplement, 1921. The total number of children under fifteen years of age rose to a maximum in the early part of the last war and has been falling ever since except for the brief rise which immediately followed the last war. The figures of total population at the top of the figure show how the proportion of children in the population has decreased.

Death-rates from all causes

Table 1 shows the annual death-rates from all causes per 1,000 living at all ages and in various age groups of childhood from the decennium 1841–50 to 1943. It is not possible to give all the recent figures because some are not available after 1940, but Stocks (1943 and 1944a) has made it possible to form an accurate picture of the trends of the rates in childhood during this war.

TABLE 1

ENGLAND AND WALES: DEATH-RATES
1841–50—1943

(Rates per 1,000 living in each age group, Infant Mortality per 1,000 Births)

	All ages (Standard:)	0–	5–	10–15	Infant mortality	1–5 years
1841–50	21·6	66·0	9·0	5·3	153	
51–60	21·2	67·6	8·5	5·0	154	(?)36·1
61–70	21·3	68·6	8·0	4·5	154	36·3
71–80	20·3	63·4	6·5	3·7	149	31·2
81–90	18·6	56 ·8	5·3	3·0	142	27·0
91–1900	18·1	57·7	4·3	2·5	153	24·3
1901–10	15·2	46·0	3·6	2·1	128	18·4
11–15	13·7	37·5	3·4	2·1	110	16·2
16–20	13·4	31·4	3·8	2·5	90	14·6
21–25	10·9	24·4	2·5	1·7	76	10·3
26–30	10·3	20·8	2·4	1·6	68	8·6
31–35	9·6	18·1	2·2	1·4	62	6·6
36	9·2	17·0	2·0	1·2	59	5·5
37	9·2	16·7	1·9	1·2	58	5·1
38	8·5	15·3	1·9	1·2	53	4·6
39	8·5	13·7	1·5	1·0	50	3·5
40	9·9	15·6	2·0	1·4	56	4·8
41	9·3		2·1	1·4	59	5·3
42	8·1		1·5	1·0	51	3·4
43	8·2		1·4	1·0	49	3·3

Figure 2 is intended to facilitate comparison of the rates of change of death-rates in the different age groups. It has been plotted on logarithmic graph paper instead of on ordinary arithmetic graph paper because this method of plotting gives a better picture of the general trend of rates and because it is easy, by this method, to compare the trend of rates which have widely different absolute values.

As the method may be unfamiliar a simple example may be desirable. Suppose it is desired to show graphically the behaviour of two diseases A and B. A has rates in successive periods of 200, 100 and 50 per million living. B is a less common cause of death and in the same successive periods has rates of 40, 20 and 10 per million living. Figure 3a shows the result of plotting these rates on ordinary graph paper and figure 3b the result of plotting on logarithmic graph paper. The arithmetic graph (3a) gives the impression that A is declining faster than B whereas the rate of decline is really the same, one-half for both experiences. On the logarithmic graph (3b) the rate of decline is clearly seen to be the same.

In figure 2 the continuous lines represent the rates in the age groups 0–5, 5–10, 10–15 years, and the dotted lines represent a further analysis of the rate 0–5, i.e. the infant mortality rate per 100 births and the rate in the age group 1–5. It is clear that the rate 0–5 follows much the same trend as that of infant mortality, but the rate 1–5 follows a rather

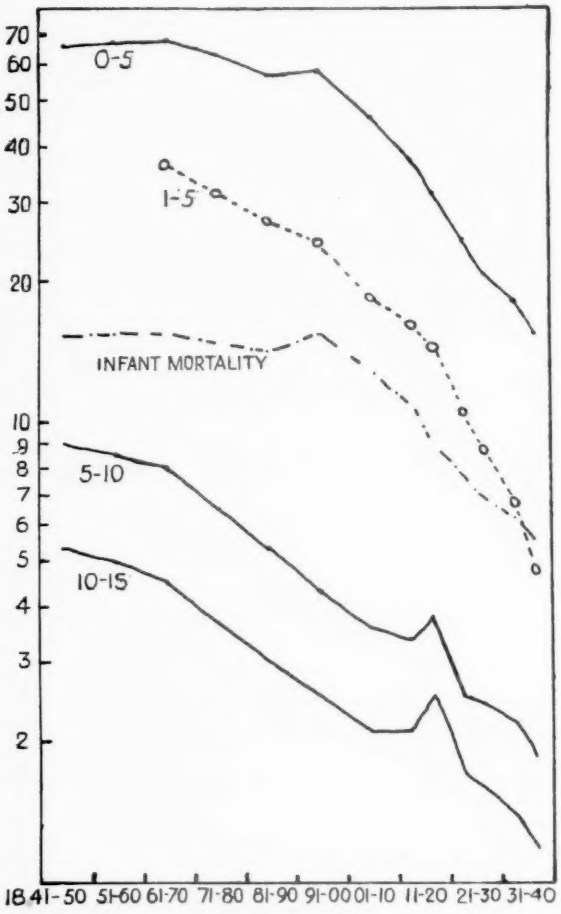

FIG. 2.—England and Wales: Death rates (per 1,000 living) in different age groups of childhood. Infant mortality (per 100 births). 1841–50 to 1931–40. Logarithmic scale.

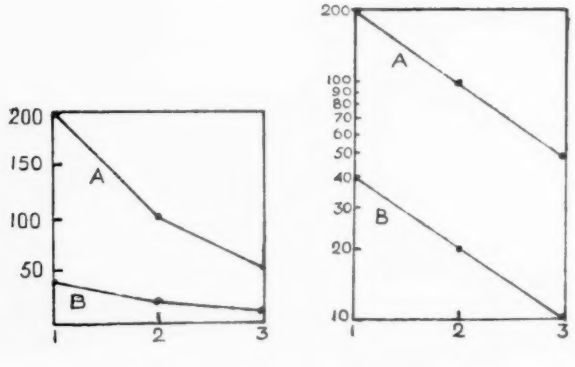

FIG. 3.—Graphs to show difference between plotting on ordinary (arithmetic) and logarithmic graph paper.

different course. Infant mortality did not begin to fall until about 1900, but since then the fall has been continuous and fairly steady. The rate in the age group 1–5 was almost stationary between 1840 and 1870 and began to fall in the decennium 1871–80. It fell slowly at first but more rapidly from about 1900 and rapidly from soon after the last war to the present time. The rates for older children show a slow fall for about the first thirty years then a more rapid fall arrested in the quinquennium 1911–15 and rising in the quinquennium 1916–20. This rise was chiefly due to the pandemic of influenza of 1918 and is more marked in the 10–15 curve than in the 5–10 curve. After the last war the fall continued and was accelerated from about 1935. Figure 4 shows the course of events in different age groups from 1911 to the present time in greater detail. It will be seen that while the rates of 0–1 (infant mortality), 1–5, 5–10 and 10–15 have all been falling more or less continuously from 1918, they have not all fallen at the same speed or in the

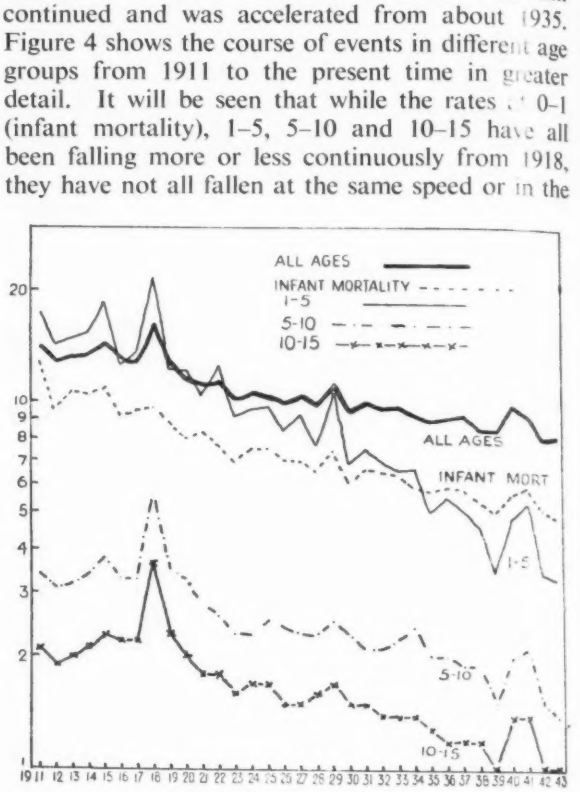

FIG. 4.—England and Wales: Death-rates from all causes at all ages (stand.); Age group 10–15; 5–10; 1–5; infant mortality (per 100 births). Rates per 1,000 living. Individual years 1911–43. Logarithmic scale.

same way. The peaks in 1918 were chiefly due to the pandemic of influenza and it is interesting to note that the rates for older children were affected most and the infant mortality rate hardly at all. The high infant mortality in 1911 was due to diarrhoea coincident with a hot summer, but after 1911 epidemics of diarrhoea decreased in severity and the last one noticeable on the curve of infant mortality from all causes is that of 1921 (see also fig. 18). The peaks on the 1–5 curve were due to high rates from broncho-pneumonia, measles and whooping-cough occurring alone or in combination. The fluctuations of the 5–10 and 10–15 curves were associated chiefly with variations in the mortality of diphtheria. The low levels for 1939 and 1942 are obvious. It is not easy to be sure of any marked correspondence of trend in the different curves, except for the general downward one, but there is a suggestion of a rapid fall after the last war followed by a period of arrest or slower fall and then another rapid fall from about 1934.

Course of death-rates from principal causes

So far the rates from all causes have been considered. Table 2 compares infant mortality per

1,000 births from principal causes in 1873–75 with infant mortality in 1931–35 and death rates from the principal causes in different age groups of childhood (1–5, 5–10 and 10–15) in 1861–70 with those in 1931–35. It is impossible to discuss all the changes in medical knowledge and in methods of classification which may have affected comparability between the earlier and the later figures, and it is not intended that the table should be regarded as more than a rough comparison of the relative importance of different causes at two widely separated epochs. There are, however, certain features so obvious that they must be due to real changes. In the figures of infant mortality an attempt has been made to separate the deaths due to conditions peculiar to early infancy, roughly corresponding to neonatal mortality, from those due to infections. It is, however, well known how difficult it is, even now, to separate infant deaths into these two main groups and it is much more difficult to do this for deaths which occurred many years ago. If it is assumed that the deaths after the first month from prematurity and allied causes roughly cancel out the deaths during the first month from infections, the neonatal rate in 1873–75 was 40·9. Applying the same line of reasoning to the figures for 1931–35 the neonatal rate works out at 29·03, whereas the actual figure for the later period, calculated from the number of deaths which really occurred under four weeks, was 31·4. The true neonatal rate is not available for the earlier period.

The great importance of the indefinite group of lung diseases, chiefly bronchitis and pneumonia, and particularly among younger children, is obvious both in the earlier and in the later figures. Another indefinite group which caused a high mortality among young children in the earlier period is that of ' brain diseases.' These deaths appeared largely under the sub-heading of ' convulsions.' It is impossible to say what were the true causes of these deaths, but probably the minority were due to true disease of the central nervous system and the

TABLE 2

Infant mortality per 1,000 births	England and Wales: Death-rates per million living 1861–70		
England 1873–75	1–5	5–10	10–15
Lung diseases .. 26·3	Lung Diseases .. 639	Scarlet fever .. 219	Tuberculosis .. 110
Convulsions .. .. 25·1	Scarlet fever .. 537	Tuberculosis .. 98	Typhus 71
Diarrhoea .. .. 17·1	Tuberculosis .. 382	Typhus 92	Scarlet fever .. 50
Tuberculosis .. .. 9·8	Brain diseases .. 312	Diphtheria 39·5 } 64	Violence 45
Whooping-cough .. 5·9	Measles 307	Croup 24·9 }	Brain diseases .. 33
Teething .. .. 2·9	Whooping-cough .. 277	Brain diseases .. 57	Lung diseases .. 21
Measles .. .. 2·2	Diphtheria 83 } 255	Lung diseases .. 55	(Bronchitis and pneumonia 15)
Scarlet fever .. 1·4	Croup 172 }	(Bronchitis and pneumonia 44)	Diphtheria 13·7 } 15
Atrophy .. .. 26·7	Diarrhoea and dysentery .. 193	Violence 46	Croup 1·3 }
Prem. birth .. .. 12·8	Typhus 137	Measles 24	Smallpox 6
Suffocation .. .. 1·4	Violence 98	Whooping-cough .. 15	Measles 3
Other causes .. .. 21·1	Smallpox 47	Smallpox 15	Whooping-cough .. 1
All causes .. .. 152·7	All causes 3, 634	All causes 799	All causes 449

England and Wales: 1931–35	1931–35		
	1–5	5–10	10–15
Bronchitis and pneumonia .. .. 12·2	Bronchitis and pneumonia (201) 191	Diphtheria 42	Tuberculosis 20
Diarrhoea and enteritis .. .. 5·4	Measles (76) .. 80	Violence 30	Violence 20
Convulsions .. .. 1·9	Tuberculosis (60) .. 60	Bronchitis and pneumonia .. 20	Bronchitis and pneumonia .. 10
Whooping-cough .. 1·7	Diphtheria (46) .. 47	Tuberculosis .. 20	Heart disease .. 10
Measles .. .. 0·9	Whooping-cough (44) 48	Measles 10	Diphtheria 10
Tuberculosis .. .. 0·8	Violence (44) .. 44	Heart disease .. 8	Nephritis 4
Prem. birth .. .. 18·0	Diseases of C.N.S. .. 33	Scarlet fever .. 6	Scarlet fever .. 2
Congenital malf. .. 5·9	Diarrhoea and enteritis 25	Nephritis 3	Measles less than .. 1
Congenital debility .. 2·9	Cerebrospinal fever 10	Whooping-cough .. 3	Whooping-cough less than 0·5 .. .. 0·5
Injury at birth .. 2·3	Scarlet fever .. 10		
All causes .. .. 62·2	All causes 656	All causes 220	All causes 130

Figs. in brackets are according to 1940 method of classification.

majority were due to other infections. As a recorded cause of death 'convulsions' has been decreasing steadily as certification has improved. Scarlet fever which used to be such a terrible scourge among children, particularly among those of school age, is no longer an important cause of death. The death-rates from other common infectious diseases have decreased considerably and so have those from tuberculosis and the intestinal infections.

The next two figures (5 and 6) show the trends, on a logarithmic scale, of death-rates of certain diseases or groups of diseases. For the common infectious diseases (fig. 5) the rates for the whole age period 0–15 have been chosen because these rates are easily available. For bronchitis and pneumonia, diarrhoea, tuberculosis and smallpox

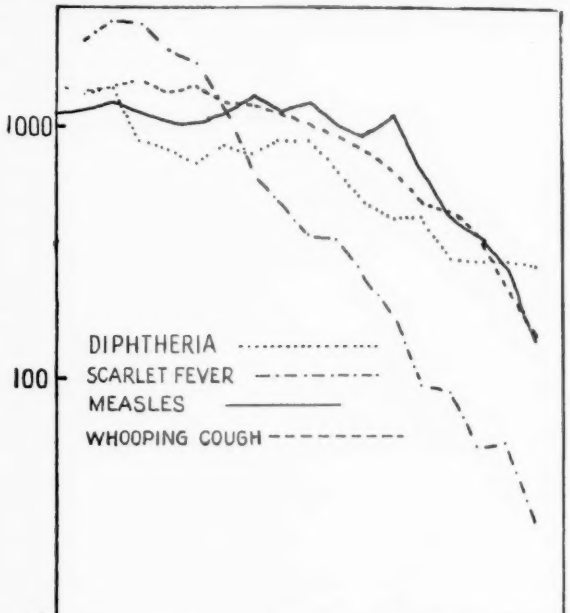

FIG. 5.—England and Wales : Age group 0–15. Death-rates (quinquennial periods) per million living from common infectious diseases. Logarithmic scale.

(fig. 6) the rates in the age group 0–5 have been used. Fig. 5 brings out the point, which is not clear on an ordinary arithmetic graph, that the death-rate from scarlet fever has been decreasing rapidly and continuously since about 1875 except for three short periods of arrest. The death-rates of most of the infections of childhood began to decline about the beginning of the century, but smallpox and scarlet fever began to decline earlier and measles rather later. Rates for all diseases except diphtheria have continued to fall, but the recent history of that disease will be considered later.

Figures 7 and 8 show the trends of death-rates from important infections in the age group 1–5 from 1911 to 1942. Fig. 7 is constructed from averages of the rates over four-year periods because the diseases shown vary so much from year to year that a graph showing rates for each year separately would be very confusing. The diseases shown in fig. 8 do not vary so much in incidence from year

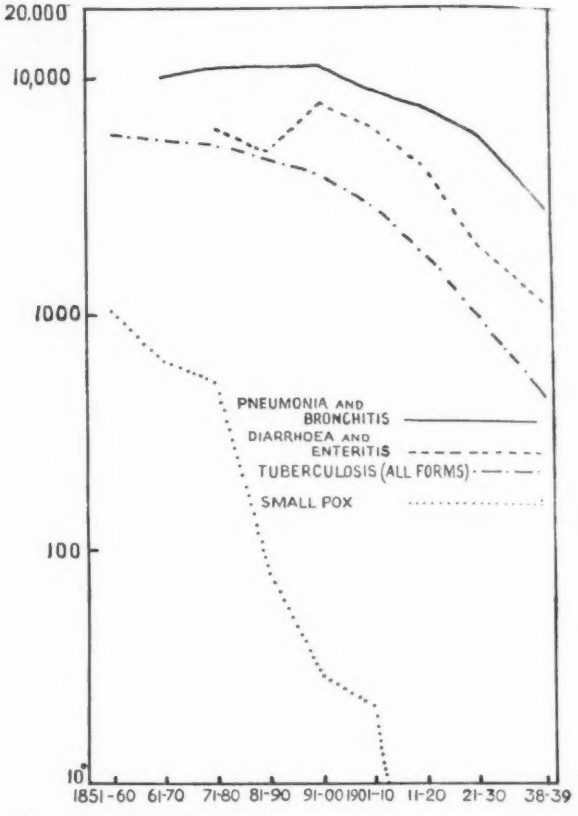

FIG. 6.—England and Wales : Age group 0–5. Death rates per million living from bronchitis and pneumonia; diarrhoea and enteritis; tuberculosis (all forms); smallpox. Decennial periods except for last point—1938–39. Logarithmic scale, 1851–1939.

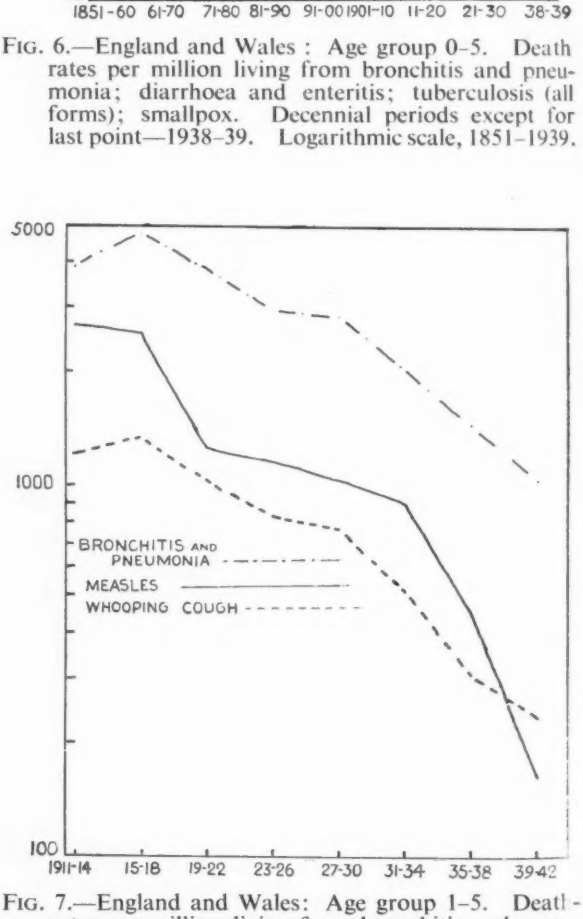

FIG. 7.—England and Wales: Age group 1–5. Death-rates per million living from bronchitis and pneumonia; measles; whooping-cough. Averages of annual rates over four-year periods. Logarithmic scale, 1911–1942.

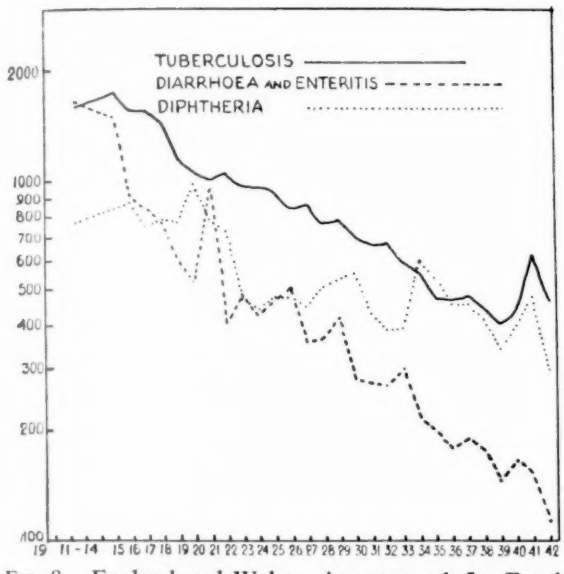

FIG. 8.—England and Wales: Age group 1–5. Death-rates per million living from tuberculosis (all forms); diphtheria and enteritis. First point is rate for 1911–14 and subsequent rates are annual 1911–14 to 1942. Logarithmic scale.

to year and so annual rates are shown. Both graphs are on logarithmic paper. The rates for the years of the last war are taken from the Registrar-General's annual reports for those years, those from 1921 to 1935 from the Registrar-General's Annual Review (Text) 1937, and those for recent years from Stocks (1943). The three series are not strictly comparable but the inaccuracies are so small that they do not affect the general picture, and it seemed better to use rates as they appeared in the Registrar-General's reports than to attempt complicated adjustments. It is difficult to be sure of any common trend in curves which differ considerably, but there is perhaps a common tendency to fall after the last war, then a period of arrest, particularly well marked in the measles curve, and a further fall.

The history of individual diseases

As an introduction to the study of individual diseases it may be of interest to describe the general picture of epidemic disease in this country as it appeared to Simon (1890) during his period of office as Medical Officer of the Privy Council, 1858-72.

When he first entered on his duties (1858) 'diphtheria had recently begun to be a source of much alarm to the public and of great interest to the medical profession as a disease which (though it had been experienced in former times) was well-nigh unknown to the existing generation of British medical practitioners.' He also mentions outbreaks of typhus (1862–63) associated with distress in the cotton towns, and a 'strange' disease spreading epidemically in Northern Europe. 'This was cerebrospinal meningitis—a febrile nervous affection of an extremely painful and dangerous kind, which was in England had hitherto hardly heard named and which on the continent had been but recently identified.' In 1865 the fourth pandemic of Asiatic cholera invaded Europe and spread to England. In addition to these special subjects of inquiry the medical department under the Privy Council carried out investigations of the high fatality of diarrhoea (1859) and of infant mortality (1861) in certain industrial towns and in East Midland (1863) agricultural districts. These were special inquiries and throughout the period various epidemics of the more common diseases—generally enteric fever, typhus or scarlatina—were investigated.

A mere glance at table 2 will show that more children have died from bronchitis and pneumonia since 1861 than from any other of the causes shown and it would be logical to begin the study of disease groups with them, but the group is ill-defined and little is known about incidence. It therefore seems better to begin with the common infectious diseases —measles, scarlet fever, diphtheria and whooping cough, and to consider first mortality rather than incidence because there is less statistical information about incidence than about mortality and it begins much more recently. Figures of mortality which are easily available date from the quinquennium 1851–55 whereas those of incidence, for England and Wales as a whole, start in 1911 for diphtheria and scarlet fever and only in November 1939, for measles and whooping-cough.

Mortality. Fig. 5 shows, on a logarithmic scale, the death-rates per million children living under fifteen years of age from 1851 to 1940. Those for diphtheria include those of 'croup,' as there was considerable confusion about the classification of deaths from diphtheria up to the end of the nineteenth century. In his Decennial Supplement 1921, the Registrar-General says:—

'In the first twenty years of civil registration there is no doubt that diphtheria did not prevail extensively as an epidemic disease in England and Wales. Prior to 1855 it is probable that most of the deaths ascribed to croup were not due to diphtheria and from 1910 on the deaths ascribed to it were not mainly due to diphtheria but between those two dates many were.'

The reduction of the death-rate from scarlet fever is the most remarkable feature of fig. 5, but the curve of measles is only a little less remarkable for the rate was almost exactly the same in the quinquennium 1911–15 as it had been in the quinquennium 1851–55, but by the quinquennium 1936–40 it had fallen to about one-eighth of its value in 1911–15. The death-rate of whooping-cough declined fairly steadily after 1880, but the decline was greatly accelerated after the last war. As both measles and whooping-cough are rarely fatal after the age of five and vary greatly in prevalence from year to year, their recent history can best be traced in figs. 7 and 11. The earlier part of the curve for diphtheria and croup (fig. 5) is suspect because of the statistical difficulty already mentioned, but from about 1900 there was a steady fall, a plateau in the years of the last war, a sharp fall from 1921–25 and then another plateau lasting up

to the very recent fall (1942–43) which is shown in fig. 9. The recent history of the four common

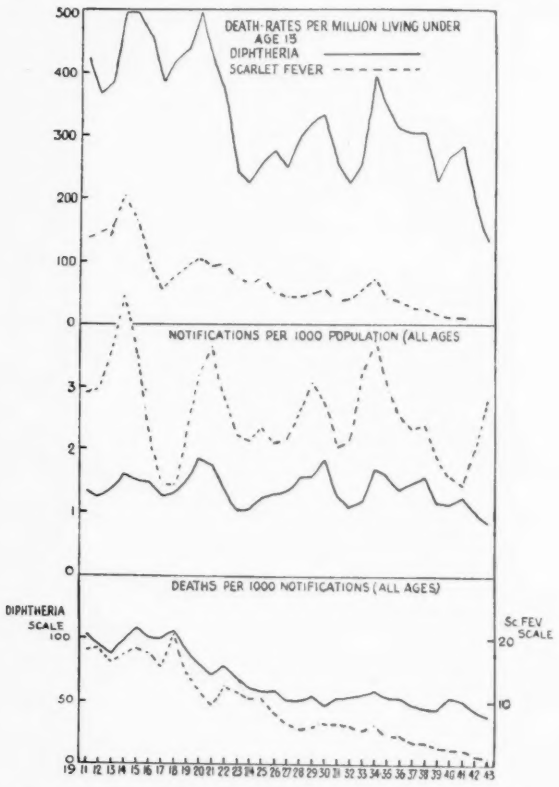

FIG. 9.—England and Wales: Diphtheria and scarlet fever. Mortality; incidence; case fatality, 1911–43.

infectious diseases is shown in table 3 taken from Stocks (1943).

Rates for 1943 are not available as yet in the same form as those given in the table but the figures of deaths at all ages published in the Registrar-General's Quarterly Returns indicate that the rates for 1943 are likely to be somewhat as follows:—

Measles—higher than in 1942, which was a non-epidemic year, but lower than in 1941.

Whooping-cough—higher than in 1942 but not so high as in 1939.

Scarlet fever—about the same as in 1941.

Diphtheria—this rate is likely to show the most striking reduction and to be substantially below the low records of 1942.

The distribution of deaths. There is one important feature of death-rates from infectious disease which has been described by the Registrar-General (Text 1937) and is discussed by Russell (1943) particularly in diphtheria but may apply to the other diseases also. This is the age-shift of mortality from the younger to the older ages. In 1906–10 and 1931–35 the comparative death-rates from diphtheria at ages may be expressed thus :—

TABLE 4

DIPHTHERIA: DEATH-RATES IN AGE GROUPS 0–5 AND 10–15 EXPRESSED AS PERCENTAGE OF THE RATE IN AGE GROUP 5–10

	1906–10	1931–35
0–5	163	95
5–10	100	100
10–15	15	24

There is some evidence in the recent figures (Stocks, 1944a and Ministry of Health, 1944) that extensive immunization of children between the ages of one and fourteen is lowering the death-rates at those ages, whereas the rates for children under one and for persons over 15 are unaffected.

Cheeseman, Martin and Russell (1939) have expressed the view that this movement of mortality of diphtheria to older ages may have been due to a considerable extent to the reduction of family density resulting in a later age of infection. Russell (1943) develops the idea in his recent survey of the epidemiology of diphtheria in the last forty years. If this explanation of the change in diphtheria mortality is true it seems likely that a similar process may have affected the death-rates of measles and whooping-cough. Both these diseases are, practically speaking, fatal only to children under school age and so any postponement of the age of infection would lead to general reduction of mortality. The measles rate fell suddenly from about 1915 and there was some acceleration of the rate of fall of the death-rate of whooping-cough about the time of the last war though this is not so clearly marked as with measles because the rate of whooping-cough had been falling steadily for many years. Hilda Woods (1933) described a similar age shift in the mortality of scarlet fever between 1901 and 1921.

When considering diseases which vary so much in incidence as do the common infectious diseases of childhood it is clearly necessary to study death-rates and incidence together before drawing any conclusions about fatality. This is particularly true of measles and whooping-cough because they have large short-term fluctuations of incidence, but unfortunately it is not possible to study incidence of these two diseases before November, 1939. It is

TABLE 3

DEATH-RATES PER MILLION LIVING (1–5) FROM COMMON INFECTIOUS DISEASES 1931–35 TO 1942

Cause	1931–35	1936	1937	1938	1939	1940	1941	1942
Measles	758	759	276	419	71	208	273	111
Whooping-cough ..	444	382	330	221	221	128	475	133
Diphtheria	457	455	454	414	342	398	482	303
Scarlet fever ..	100	73	57	57	30	19	25	12

less true of scarlet fever and diphtheria, but even they show substantial fluctuations which tend to follow the same course and to show an irregular periodicity. Fig. 9 shows how incidence, mortality and fatality of diphtheria and scarlet fever have been related since 1911. As figures for notifications divided into age groups are only just available for the whole country, the graphs of incidence and case fatality relate to the whole population. In a way the top graph may be described as the resultant of the two lower ones for obviously the death-rate of a disease depends on two factors—how common it is and how fatal. The fatality of both these diseases declined by about half between 1919 and 1927, but the death-rate did not follow quite the same trend because prevalence of both diseases was rising substantially in 1919 and 1920 and reached a peak for diphtheria in 1920 and for scarlet fever in 1921.

There is one particularly puzzling feature of the figures of notifications of these two diseases and that is their constancy over a period when the relative proportion and even the actual number of children in the population was falling considerably. Figures of notification are notoriously unreliable and there has been an increasing tendency to notify doubtful cases of diphtheria (there is inadequate provision under existing administrative arrangements for correcting wrong initial diagnosis but steps are being taken to alter this), but it seems doubtful if scarlet fever is notified more freely now than formerly. Figures of notifications for some of the larger cities go back further than the national statistics and for a number of years the Medical Officer of Health of Liverpool (1938) has given graphs showing the incidence of diphtheria and scarlet fever in the city since 1890. These graphs show fluctuations similar to those in fig. 9 but, on the whole, the notification rate for diphtheria has been on the increase and that of scarlet fever has remained the same. The evidence as to the incidence of measles is even less satisfactory because the disease has been generally notifiable for so short a time, but the number of cases reported from the schools has not changed materially from epidemic to epidemic (Brincker, 1938; London, 1927–36). Such evidence as there is, therefore, suggests that diphtheria, scarlet fever and measles are no less prevalent now than they were at the beginning of the century.

In 1942 there was a definite and most unusual movement downward of the diphtheria notifications at a time when the scarlet fever notifications were rising. This is clearer on the short-term graph (fig. 10).

Russell (1943) has critically examined the evidence that large-scale immunization against diphtheria in the United States and in Canada has affected the morbidity and mortality rates. He concludes that ' there is very strong evidence that immunization, particularly since the inclusion of the pre-school children, has reduced the morbidity and mortality from diphtheria in New York City and in Toronto.' Until recently immunization had not been practised in this country to an extent which would justify the search for signs of it in the national statistics, but by December 31, 1942, it was estimated that rather more than half the children under 15 in England and Wales had been immunized (Ministry of Health, 1944).

The recent history (1938–43) of the four common infectious diseases is given in fig. 10 which shows weekly notifications and deaths at all ages. The approximate position of school holidays and of the period of school closure in evacuation areas in 1939–40 has been indicated. The effect of school closure and of school holidays is obvious. Stocks (1941, 1942) has examined in detail the effect of dispersal on the incidence of all four diseases. He found that the incidence of diphtheria and scarlet fever was substantially reduced in the evacuation

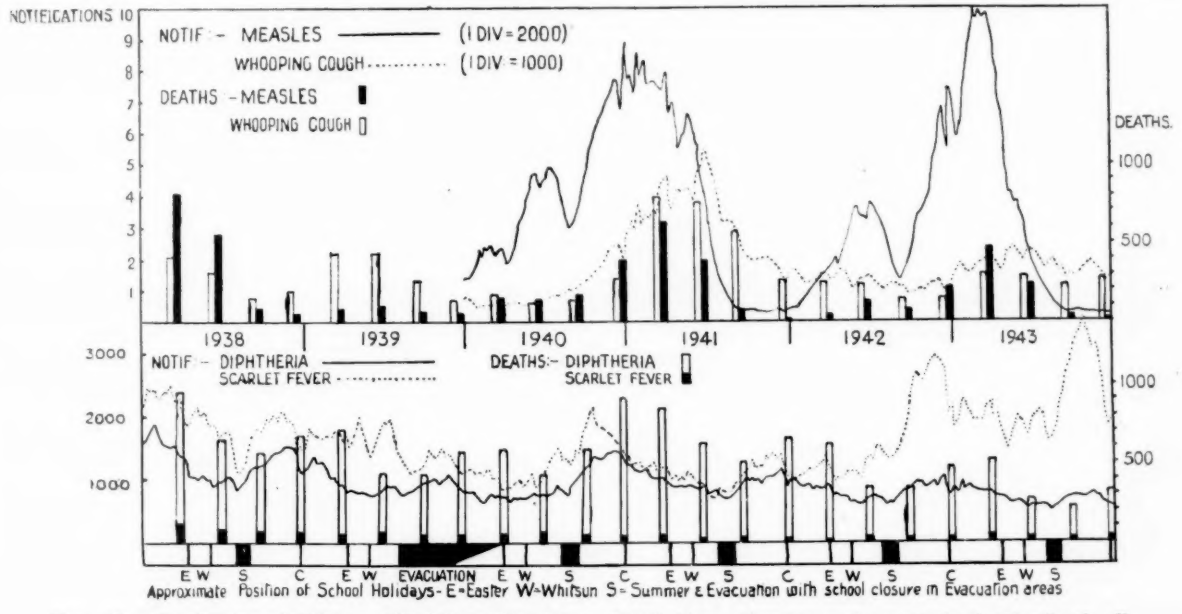

FIG. 10.—England and Wales: Weekly notifications of infectious diseases and quarterly deaths (both all ages). 1938–1943.

areas and was increased in the reception areas. It was less easy to determine the effect of dispersal on the incidence of measles and of whooping-cough because of the absence of figures of notifications for previous years, but the evidence suggested strongly that dispersal disturbed the usual periodicity of measles and reduced the incidence of whooping-cough in the evacuation areas. The evacuation areas contained so large a proportion of the child population that the national figures shown in fig. 10 show chiefly what was happening in those areas.

Pneumococcal and streptococcal infections. It is well known that nearly all deaths ascribed to measles or to whooping-cough are due to complications rather than to the disease itself and that most of the complications are either pneumococcal or streptococcal infections. Fig. 11 shows the annual

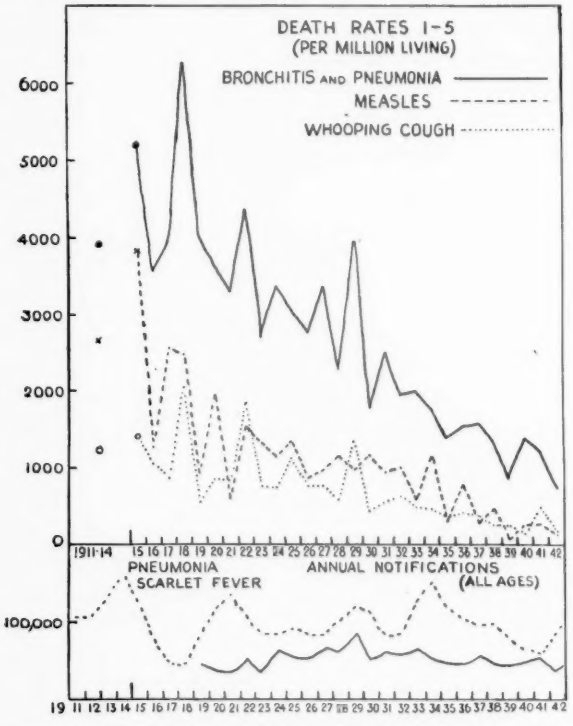

FIG. 11.—England and Wales: Death-rates per million living in age group 1–5. 1911–14 to 1942 from bronchitis and pneumonia; measles; whooping-cough. Notifications of pneumonia and scarlet fever.

death-rates from measles, whooping-cough and bronchitis and pneumonia in the age group 1–5 and the annual notifications of scarlet fever at all ages. It is intended to show the relationship of the short-term fluctuations of the different diseases. Whooping-cough and bronchitis and pneumonia have the same peaks of mortality—in 1918, 1922 and 1929—though whether this is due to a true association of the two or to difficulties of differential diagnosis is uncertain. Measles has such irregular oscillations and the rate is so different in epidemic and in non-epidemic years that it is difficult to make any generalization about it, but there is perhaps a tendency for the rate to be high when notifications of scarlet fever are also high. For description of the trend of death-rates it is convenient to separate pneumococcal and streptococcal infections, but the distinction is not clear-cut because clinical classifications, on which death certificates are based, do not correspond with etiological classifications.

PNEUMOCOCCAL INFECTIONS. In the year 1939, which was a year of remarkably low mortality from infections in childhood, 17 per cent. of all deaths occurring in children under 15 years were ascribed either to bronchitis or to pneumonia, and in 1940 the corresponding figure was 21 per cent. Throughout the period under review bronchitis and pneumonia have been the most important causes of death in children under five and have been among the most important causes in older children (see table 2). The way in which the rates in different age groups have fallen since 1861–70 is shown in fig. 12. The rates for the age groups 5–10 and 10–15

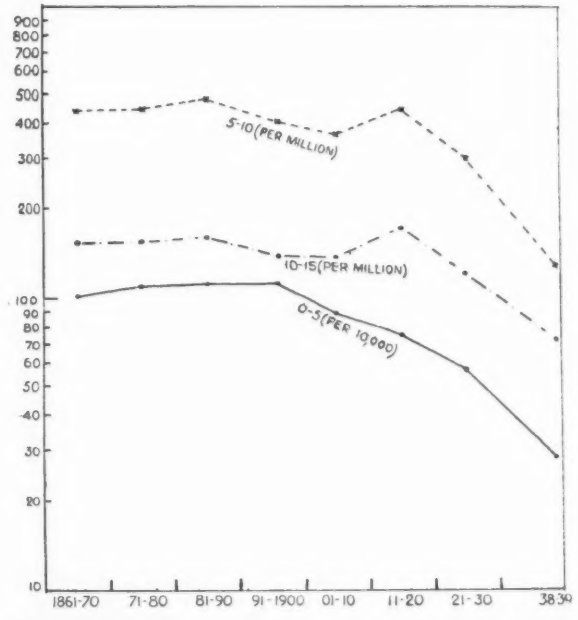

FIG. 12.—England and Wales: 1861–70—1938–39. Death-rates from bronchitis and pneumonia in different age-groups. Logarithmic scale, rates 10–15 and 5–10 per million; 0–5 per 10,000.

began to fall rather earlier than that for the age group 0–5 but rose in the decennium 1911–20. This rise was probably due to the pandemic of influenza in 1918 which affected the death-rates of older children more than those of younger ones. Fig. 13 describes the recent behaviour of pneumonia and influenza and notifications of scarlet fever have been included to serve as a link with fig. 14 which is concerned with certain streptococcal diseases. Fig. 13 shows how closely interrelated are the rates for influenza and for bronchitis and pneumonia though it is impossible to say how far this is due to difficulties of diagnosis and how far it is due to a true association of different diseases. It should be noted that only acute primary and influenzal pneumonia are notifiable diseases, so that notifications do not give a complete picture of the incidence of all forms of pneumonia.

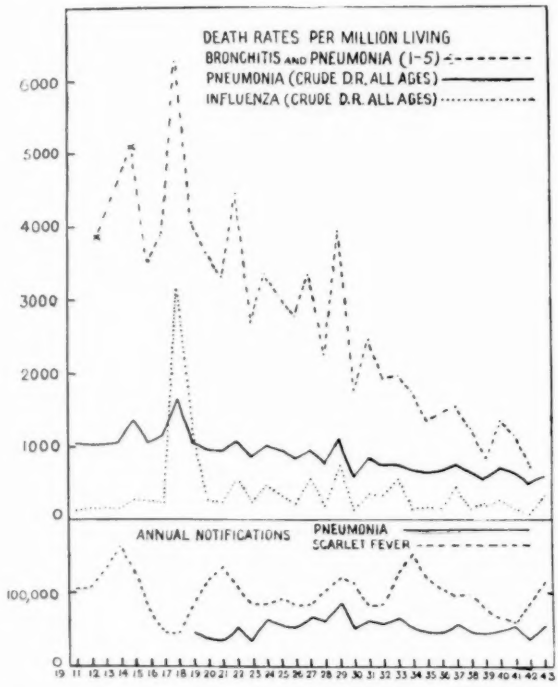

FIG. 13.—England and Wales: Crude D.R.s per million from pneumonia (all forms) and influenza; D.R. from bronchitis and pneumonia (age-groups 1–5, per million living), 1911–43. Annual notifications of pneumonia and scarlet fever.

STREPTOCOCCAL INFECTIONS. It is, unfortunately, impossible to give even an estimate of the total number of deaths among children due to streptococcal infections. Allison (1942) says 'the haemolytic streptococcus is probably the most dangerous of the common infecting agents and is certainly the most protean in the diseases it produces.' These generalizations are particularly true in their application to children, but, because of the difficulty of selecting diseases which are predominantly streptococcal in origin and also affect children rather than adults, fig. 14 shows crude death-rates at all ages from certain predominantly

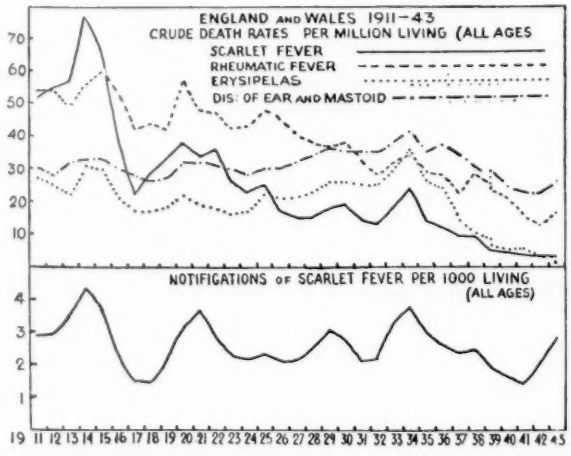

FIG. 14.—England and Wales: Crude death-rates (all ages) of certain predominantly streptococcal diseases, and notification rates of scarlet fever: 1911–43.

streptococcal diseases together with notification rates of scarlet fever. Although the association is not perfect there is sufficient evidence to suggest that death-rates from streptococcal diseases generally tend to move up and down together and to be associated with changes in the prevalence of scarlet fever. The wave of streptococcal activity which had its peak in 1934 is an obvious example of association. Puerperal sepsis has been omitted from the figure partly to avoid confusion and partly because changes in methods of classification make it difficult to construct a satisfactory long-term curve. There is no doubt, however, that the death-rate from puerperal sepsis has followed a similar course to the diseases shown. It is justifiable, therefore, to regard notifications of scarlet fever as a sort of biological indicator of streptococcal activity generally and so these notifications have a value which is not affected by any argument as to their value in the control of the disease itself.

Rheumatism. Juvenile rheumatism has been the object of many detailed studies and here it is appropriate only to summarize the main facts and to try to put them in relation with the facts about other infections which have already been given.

The death-rate from rheumatic fever per million living in the age group 10–15 fell from about 100 in the decennium 1891–1900 to about 47 in 1937, and there has been a further decline since then though it is not possible from the published figures to state it in exactly the same terms. The death-rate from rheumatic fever does not, however, give a complete picture of the mortality of the disease because deaths due to valvular disease of the heart are ascribed to rheumatism only when it is stated on the certificate that active disease was present at the time of death. A modification of Glover's (1943) graph (fig. 15) of the numbers of deaths under 15 years of age from rheumatic fever, from heart disease and from scarlet fever from 1928 to 1941 gives a better picture of the recent fall for, as he says, it may be assumed that at least nine-tenths of the deaths ascribed to heart disease in this age group are due to rheumatism. Of the exact numbers of children who have damaged hearts as a result of rheumatism there is no exact information, but it is known that something like half the children in schools for physically defective children are cardiac cripples. These are only the more serious cases and there must be many children leading more or less normal lives and attending ordinary schools who have suffered some damage. The proportion of children in schools for physically defective children who are admitted because they have heart disease has been increasing for many years; not because the absolute number of them has been increasing but because greater care has been taken to detect cases and to give them suitable education. Glover (1930) described rheumatic fever as an obsolescent disease and subsequent events have tended to confirm that view. It is of interest to note that although the sulphonamides are of doubtful value in the treatment of rheumatism the decline

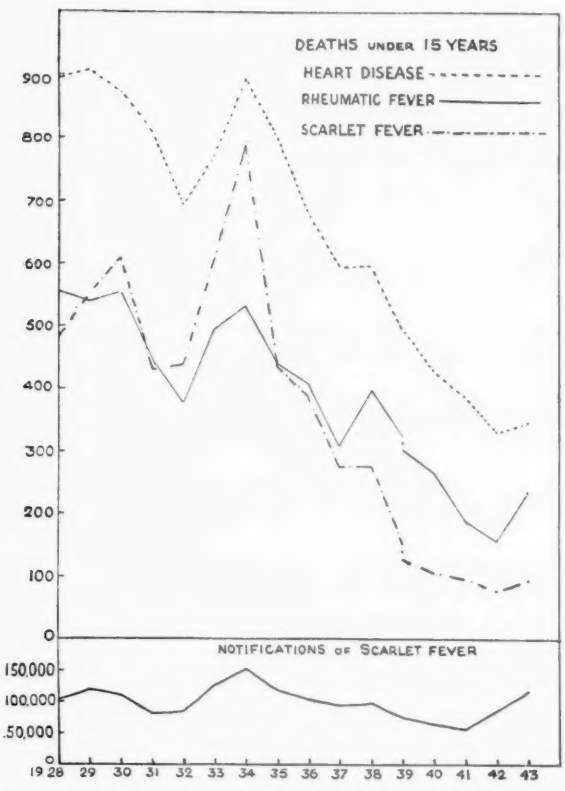

FIG. 15.—England and Wales: Deaths from heart diseases, rheumatic fever, scarlet fever at ages under 15 years. Notification of scarlet fever (all ages): 1928–43.

has been particularly rapid recently and has been comparable with that of the diseases for which sulphonamides are effective. Some of this decline is due to the fact that streptococcal activity generally was at a low level in 1939–40, and the slight increase in activity which has occurred recently has caused a slight increase in deaths from rheumatism (fig. 15). This is probably only a comparatively small and temporary effect and not important in comparison with the long-term reduction of mortality.

Tuberculosis. In that part of table 2 which relates to the 'sixties and 'seventies, tuberculosis (all forms) is fourth in the list of infections in the column of infant mortality, third in the age group 1–5, second in the age group 5–10 and first in the age group 10–15. In 1931–35 the relative position of tuberculosis in the various age groups is not very different, but the rate is reduced to about one-twelfth of that in 1861–70 in the case of infants, and between one-seventh and one-fifth in the older age groups. The general trend of rates in the different age groups is shown on a logarithmic scale in fig. 16. All the rates have been falling since 1851–60, but that of the age group 0–5 fell slowly until 1891–1900, and then more rapidly. The rate in the age group 5–10 fell steadily until the last war, remained stationary in the war, and then fell rapidly. That of the age group 10–15 had much the same trend, except for a definite rise in the quinquennium 1916–20. In young children tuberculosis is like most other infections in that the death-rate of males is higher than that of females, but in the age group 5–10, the rates are much the same for both sexes, and in the age group 10–15, that of females is substantially higher than that of males. Among children under five, the deaths are chiefly due to tuberculous meningitis, whereas with increasing age, respiratory tuberculosis becomes more important as a cause of death. The behaviour of tuberculosis in this war, up to the end of 1941, and in the last one has been compared in a report by a committee of the Medical Research Council (1942). Table 5 is taken from that report, with the figures for 1931–35, 1942 and 1943 added. The average figures for 1931–35 are included to link the table with fig. 16. The principal difference between this war and the last one has been that in the last one the deaths from respiratory tuberculosis increased, while the deaths from tuberculous meningitis decreased, whereas in this war both increased to some extent.

The earlier history of tuberculous meningitis is difficult to make out with any certainty, because the disease was formerly called acute hydrocephalus and no doubt deaths due to the condition which is now known as hydrocephalus were returned under the same heading. These were probably always few in number and a more serious difficulty

TABLE 5

DEATHS FROM TUBERCULOSIS: ENGLAND AND WALES: AGE-GROUPS 0–5, 5–15: 1931–35 AND 1938–43

Year	Respiratory				Other				All Forms	
	0–5		5–15		0–5		5–15		0–5	5–15
	M	F	M	F	M	F	M	F	M+F	M+F
1931–35 Average	131	110	182	317	922	740	517	492	1903	1508
1938	92	61	101	161	649	569	355	347	1371	964
1939	79	53	69	157	596	497	337	308	1225	871
1940	73	77	97	182	657	563	330	327	1370	936
1941	133	117	112	189	853	712	418	422	1815	1141
1942	103	96	81	122	664	535	386	341	1398	930
1943	127	101	68	138	629	540	337	329	1397	872

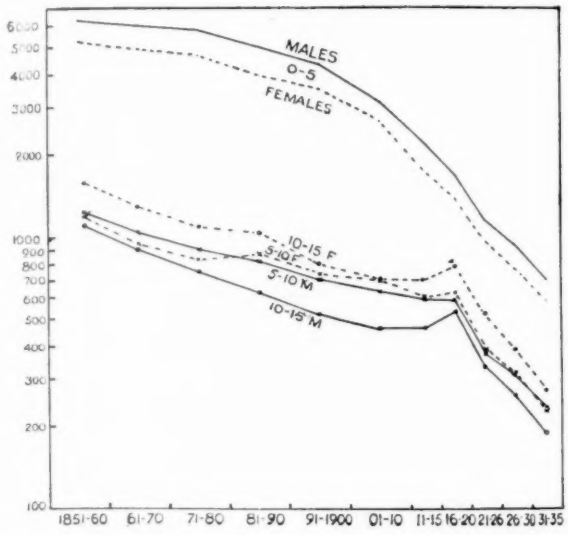

FIG. 16.—England and Wales: Tuberculosis (all forms). Death-rates per million living at various ages; Decennial periods 1851–1910, quinquennial 1911–35. Logarithmic scale.

must have been that of differentiation from other forms of meningitis, or even from a variety of other cerebral conditions. With this reservation, then, it can be said that the death-rate from tuberculous meningitis has shown a rapid and continuous decline in the age group 0–5 since 1861–70, except for the recent small rise. In the age group 5–10 the fall began about 1880, and in the age group 10–15, which has a much lower mortality than the younger ones, in 1921–25.

The death-rates from abdominal tuberculosis have fallen rapidly among children under 10 since 1881–90, but at later ages the fall did not start until 1900.

Tuberculosis of the bones and joints is different from other forms in that its importance is rather as a cause of crippling than as a cause of death. There is no doubt that the incidence of crippling due to tuberculosis has decreased very much, but it is difficult to give statistical evidence, because of the difficulty of defining 'crippling,' and because increased vigilance is liable to produce an apparent increase in the number of cases. Between 1921 and 1937, however, the number of deaths from tuberculosis of the bones and joints among children under 15 fell from 173 to 44, and between 1934 and 1938 the number of children who completed treatment in residential institutions fell from 1,965 to 1,647 (Ministry of Health, 1938).

Epidemic diseases of the central nervous system. It is convenient to consider together cerebrospinal fever, acute poliomyelitis and encephalitis lethargica, usually called the epidemic diseases of the central nervous system. They have a recorded history which begins comparatively recently. They are not, in non-epidemic years, large causes of death among children or for that matter among adults. In 1938, for example, they caused 600 deaths among children under 15 compared with nearly 1,600 due to measles. 1938 was not a year of epidemic prevalence of cerebrospinal fever but was a year of rather high endemic prevalence. The graph of crude death-rates (fig. 17) gives a good idea of the course these diseases have taken. Cerebrospinal fever has had three peaks in 1915, 1931 and 1940, the last being far the highest. Encephalitis lethargica had a peak in 1921 and a higher one in 1924 and has been slowly falling since. It should be noted that the change in the method of allocation of deaths begun in 1940 has had a substantial effect in reducing the number of deaths allocated to this disease because it is often stated as a secondary cause of death and by the rules in force before 1940 it was given a high preference over other causes. Acute poliomyelitis has had several small peaks, the last and highest being in 1938.

The relation between notification and deaths of all three diseases is interesting. In times of low prevalence the number of notifications tends to decrease more than the deaths so that the apparent fatality increases greatly. This is particularly noticeable with encephalitis lethargica. In 1937, for example, there were nearly three and a half times as many deaths as there were notifications, whereas in 1924, there were only 18·3 deaths for every 100 notifications. There was an extraordinary rise in the apparent fatality rate of acute poliomyelitis in 1918, due partly to the fact that some deaths really due to the then 'new disease'—encephalitis lethargica—were certified as polio-encephalitis and partly to a reduction of notifications unaccompanied by a corresponding reduction of deaths. Cerebrospinal fever showed a few more deaths than notifications in certain years, e.g. 1928, and up to 1937 the apparent fatality rate never

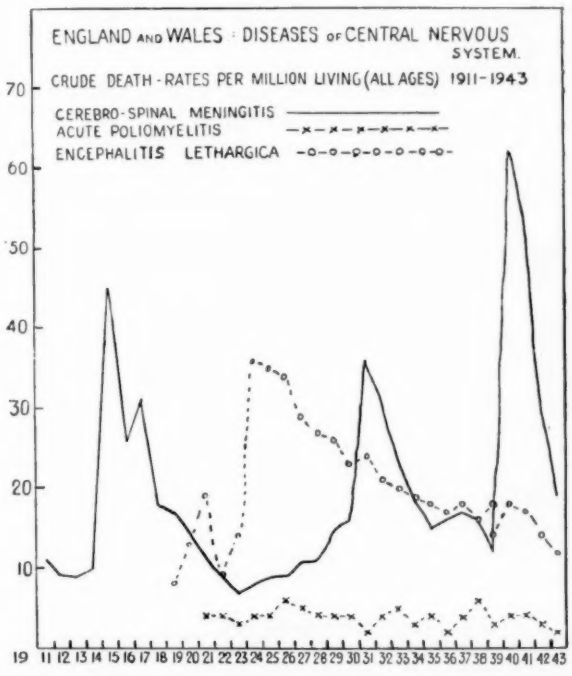

FIG. 17.

fell below 55·6 per cent. (1933). For these reasons it is necessary to treat fatality rates, i.e. $\frac{\text{deaths}}{\text{notifications}}$, with some reserve, but the recent history of cerebro-spinal fever does suggest a real and very substantial fall in fatality:—

TABLE 6

RECENT FATALITY RATES OF CEREBRO-SPINAL FEVER

			Per cent.	
1937	..	..	61·2	
1938	..	..	50·6	
			Civilians	*Non-civilians*
1939	..	..	36	16
1940	..	..	22	8
1941	..	..	21	8
1942	..	..	22	8
1943	..	..	25	10

It seems certain that this great reduction has been due to the introduction of the sulphonamides. The importance of the epidemic of 1940 may be judged by the fact that in 1940 there were 1,343 (1941–1125) deaths from cerebrospinal fever among children under 15 compared with 425 in 1938 and 310 in 1939.

All these diseases are important causes of disability. It is impossible to give any reliable statistics of the numbers crippled by them but every cripple school and every hospital and orthopaedic clinic has its quota of cases due to acute poliomyelitis and every school for the deaf has a number of children deafened by cerebrospinal fever. The child victims of encephalitis lethargica, though few in number, are among the most pathetic of all, for the mental changes cause distress to themselves and their families and they are extremely difficult to look after.

Diseases of the nervous system and sense organs. The epidemic diseases of the nervous system are not now included by the Registrar-General under the general heading of diseases of the nervous system and sense organs but under the general heading of 'Epidemic Diseases.' It is probable, however, that the actual transfer of deaths from one heading to the other has been a gradual process dependent on the growth of medical knowledge of the diseases and the spread of that knowledge among the general practitioners of the country. Cerebro-spinal fever deaths were first returned under that separate head in 1869, but the death-rates given in table 9 of the Registrar-General's Annual Review begin in 1911. Death-rates for acute poliomyelitis also date from 1911 and those from encephalitis lethargica from 1921.

At the present time deaths among children returned under the main heading 'diseases of the nervous system and sense organs' fall chiefly under three sub-headings—convulsions, meningitis (not including meningococcal or tuberculous meningitis) and diseases of the ear and mastoid sinus. In 1938, 2,584 of the total of 51,986 deaths which occurred in children under 15 were allocated to the main heading—864 of these to convulsions, 534 to meningitis and 649 to diseases of the ear and mastoid. 'Convulsions' is, of course, much more commonly stated as the cause of death in infants than in older children. Both convulsions and meningitis are indefinite causes and have been gradually disappearing from the returns as certification has improved. In the age group 1–5, for example, the death-rate from 'convulsions' per million living in 1911–14 was 460 and in 1937 it was 53, that of 'meningitis' was 451 in 1911–14 and 88 in 1937. When considering the trend of death-rates in childhood over a long period it is necessary to bear in mind this kind of effect because it is likely that the death-rates from common infectious diseases and respiratory infections were substantially understated in the earlier part of the period, particularly among infants, a large number of deaths being ascribed to this indefinite cause 'convulsions.' The deaths in children from diseases of the ear and mastoid rose in the early thirties to a maximum in 1934 and have since declined in much the same way that other streptococcal diseases have (fig. 14).

It is impossible to give a satisfactory picture of the course of these, even now, ill-defined diseases of the nervous system over the whole period because of the great changes in medical knowledge about them, but it is of interest to recall that in 1861–70 the average yearly number of deaths among children under 15 ascribed to brain diseases was 31,474 and in 1938 2,584 were ascribed to diseases of the nervous system and sense organs and another 515 to epidemic diseases of the central nervous system making 3,099 in all. These figures are not strictly comparable one with another but they serve to show what remarkable reductions have taken place in the mortality not only of the well-defined diseases which are commonly studied but also in the mortality of those conditions which, because they are ill-defined, are seldom studied.

Intestinal infections. In that part of table 2 which compares infant mortality in 1873–75 with that in 1931–35, excluding congenital causes, diarrhoea was third in the early table and second in the later one, but whereas in 1873–75 the rate was 17·1 per 1,000 births in 1931–35 it was 5·4. Fig. 18 shows how infant mortality from this cause has varied since 1885 and what relation it has had to the total rate. The last great epidemic associated with a hot summer was in 1911 and after 1915 the rate fell very considerably. There was a small and sudden rise in 1921, associated with a hot summer, but since then the rate has hardly varied from year to year and has gone down slowly from about 6·5 to just under 5·0 per 1,000 births against the rates of 30 per 1,000 which were usual in hot summers before the last war. Another feature of this disease has been the shift in mortality from the hot months of late summer to the winter months. The cause of this summer diarrhoea of infants is unknown, but from its epidemiological history it looks almost as though a disease had disappeared in the last war, except for a dying spurt of activity in 1921, and that the infantile diarrhoea of the present day, with its steady death-rate and its higher incidence in

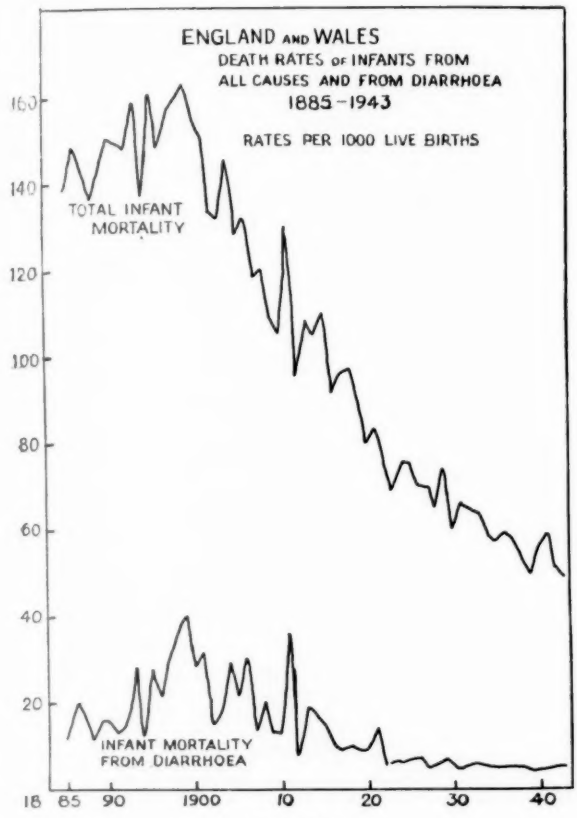

FIG. 18.

winter may have a different causation. Since 1940 enteritis deaths under two years have increased a little in the March and June quarters, but there is no sign of a return to the position of 35 years ago and it must be remembered that the population at risk has increased. The mortality rates among infants under one year during the war years have been :—1940, 4·4; 1941, 4·7; 1942, 5·0; 1943, 4·9 per 1,000 live births.

When the intestinal infections of older children are considered it is found that formerly epidemic diarrhoea and enteritis took a toll from the age group 1–5 though to nothing like the same extent as among infants. The death-rate per million living in the age group 1–5 in 1861–70 was 193 and it ranked eighth, next below diphtheria and croup. Immediately below comes typhus, which heading then included the typhoid group, and this becomes a more important cause in the older age groups—third in the age group 5–10 and second in the age group 10–15. The typhoid group was not separated from typhus until 1869. Greenwood (1935) describes the subsequent course of the standardized death-rate at all ages as follows:—

'Roughly from 1875 over the next ten years there is a rapid fall, then rather more than a decennium showing little change. At the beginning of the twentieth century another rapid fall began which slackened into a gentle descent which has continued fairly regularly since about 1910. The reader should remember that the eternal difficulty of comparability between diagnosed causes of death at different epochs probably tells against us and makes the general decline less impressive than it really is, because typhoid is now more freely diagnosed.'

Typhus has now disappeared in this country except for occasional isolated cases in the ports and the enteric group has decreased so much that in 1938 there were only 15 deaths in England and Wales in the whole age group 0–15.

In 1861–70 there were deaths from cholera in epidemic years more particularly in the later years of childhood. The last serious epidemic of this disease in England and Wales was in 1865–66 though there was danger in 1871 when the disease reached Russia and the North German ports.

The great reduction in intestinal infections as causes of death in childhood is generally considered to be the most obvious triumph of sanitary measures and this seems a reasonable explanation so far as the typhoid group and cholera are concerned, but it does not explain the behaviour of epidemic diarrhoea of infants.

Appendicitis. Mention should be made of appendicitis which caused 518 deaths among children under 15 in 1938. Between 1911–20 and 1932–34 there was no appreciable change in the standardized mortality at all ages, but there was definite evidence of postponement of death to later ages. Since 1931–35 there has been a further fall in the death-rate among young children from 67 per million in the age group 1–5 to 56 per million in 1939 and 39 per million in 1942 (Stocks, 1943). It is not clear whether this recent fall is due to a continuation of the process which was going on before or to improved methods of treatment.

Handicapped children. It would be impossible to give any general account of the part played by infections in causing disability of all degrees because these are so variable, but perhaps some rather random observations on the changes which have affected the importance of infections as causes of the major permanent disabilities may be of interest.

1. BLINDNESS. Kerr (1926) states that at the time of his first survey of the London Schools for blind children in 1903, 42 per cent. of the cases were assigned to ophthalmia neonatorum. In 1921 Bishop Harman found that about 20 per cent. of cases were due to ophthalmia neonatorum and about 21 per cent. were due to interstitial keratitis. In 1938 only 14 of 100 children in the London County Councils blind schools had been blinded by ophthalmia neonatorum and only one as a result of interstitial keratitis. Evans (1943) in a recent paper on ophthalmia neonatorum in Birmingham says that there has been only one case of blindness from this cause in the last seven years. These figures must be accepted with some reserve because it is often difficult to determine the cause of blindness from the history, but there is no doubt that there has been an enormous reduction in the number of cases due to venereal disease.

2. DEAFNESS. The great reductions of the severity

of the common infectious diseases have undoubtedly led to remarkable reductions in the number of severe cases of middle ear deafness. In an old admission register of a large school for the deaf recently examined by the author the entries during the 'seventies included a high proportion of cases due to scarlet fever and other common infectious diseases, but in the same school in 1943, there was not one case of active otitis media among 127 children. That school is probably exceptional, but there is no doubt of the enormous reduction. There is one infection, however, which is still a matter of serious concern, namely cerebrospinal meningitis, and it may be that the introduction of the sulphonamides, by reducing mortality, may indirectly increase the number of cases of deafness. Many heads of schools for the deaf have commented on the large proportions of recent admissions of children deafened by this disease, and a small preliminary investigation has been carried out by the author (Gale, 1944) which suggests an increase in the number of cases due to the disease.

Comment has already been made on the reductions of crippling by tuberculosis of bones and joints and of that due to rheumatic heart disease.

Association of bad social conditions with high child mortality

It is not, of course, a new observation that high death-rates, particularly in childhood, are closely associated with bad social conditions. This is what Farr has to say on the subject in the supplement to the 25th Annual Report of the Registrar-General covering the years 1851–60.

'There is no doubt great negligence on the part of the parents, great ignorance of the conditions on which health depends and great privation among the masses of the poor, but there is no reason to suspect that any great number of the infants in these districts fall victims to deliberate crime; yet the children of the idolatrous tribe who passed them through the fire to Moloch scarcely incurred more danger than is incurred by the children born in several districts of our large cities.'

In the supplement to the 25th report he compared the death-rates of children aged 0–5 living in 28 rural areas with the death-rates in certain great towns and found that whereas Bellingham, a rural district in Northumberland, had a death-rate of 2·3 per cent. in this age group, Liverpool had a rate of 13·2 per cent. In the Supplement to the 35th Annual Report Farr gave a table comparing the numbers of children dying under age 5 in the 'Healthy Districts' in 'England' and in 'Liverpool' and the causes of their deaths. Table 7 is an extract from this.

It was not only in cities that mortality was high and there is an interesting sidelight on infant mortality in the rural fen country in Simon's report to the Privy Council for 1863. It had been found that infant mortality in some of the fen districts, e.g. Wisbech, King's Lynn, was nearly as high as it was in the great cities, being of the order of 220–270 per 1,000 births. Dr. H. J. Hunter was sent to investigate and found that the high rate was chiefly due to maternal neglect owing to the fact that women were extensively employed in gang labour in the fields. In order to quieten the infants left behind at home it was usual to dose them heavily with an unholy brew known as 'Godfrey's cordial' which consisted of opium, treacle and oil of sassafras. The wages paid to these women working in agriculture ranged from 8d. to 1s. 8d. per day.

TABLE 7

OF 10,000 CHILDREN BORN THE NUMBER DYING UNDER THE AGE OF FIVE IN 1861–70:–

Cause	Healthy Districts	England	Liverpool
Zymotics	498	871	1,710
Tuberculosis (all forms)	146	219	318
Diseases of the brain..	227	401	498
Diseases of the lungs..	279	415	799
Other	604	726	1,279
All causes	1,754	2,632	4,604

N.B.—Farr's 'Healthy Districts' were the 51 registration districts of England and Wales which had the lowest general death-rates for years 1861–70, 17 per 1,000 and under.

Since Farr's time many investigations have been made and the problem is chiefly one of selection from a wealth of material. The earlier investigations were designed chiefly to point out the great differences obtaining in different areas, and the detailed reports on infant and on child mortality produced by the Chief Medical Officer of the Local Government Board between 1911 and 1917 are good examples. More recently attempts have been made to determine the relative importance of different social factors, but this is by no means easy because the different factors are usually so closely associated that it is difficult to isolate them. For example, bad and overcrowded housing conditions are usually associated with low incomes and large families.

The parts of the Decennial Supplements of the Registrar-General for 1911, 1921 and particularly that for 1931, which deal with Occupational Mortality give direct information on the influence of social class on the mortality of infants, for in addition to giving the mortality figures of men in different occupations, they give mortality figures of infants for different occupations of the father and for various important causes of death. The supplement for 1931 based on the mortality experience of the years 1930–32 also gives the death-rates of legitimate children in the age group 1–2 classified according to the father's occupation and for several important causes. In the summary tables the occupations of the father are classified into five great social classes. Broadly speaking, class I consists of those engaged in

the professions, class III of skilled workers and class V of unskilled and casual workers, classes II and IV being intermediate groups. It is not easy to select from the wealth of information given in this Report but the facts about the relative mortality from all causes in the different classes among infants and among children in the age group 1–2 for the years 1930–32 were (table 8):—

TABLE 8

	Infants (0–1)		Young children 1–2 per 100,000 living	
	Death-rate per 1,000 births	Percentage of rate for all classes	Rate per 100,000	Percentage of all classes
All classes..	62	100	1,452	100
Class I ..	33	53	454	31
„ II ..	45	73	728	50
„ III ..	58	94	1,258	87
„ IV ..	67	108	1,573	108
„ V ..	77	125	2,298	158

It will be seen that the difference between the classes increases with age and in a more detailed analysis of mortality at different stages of the first year this effect is shown in greater detail.

TABLE 9

ENGLAND AND WALES: 1931–32. DEATH-RATES AT DIFFERENT STAGES OF FIRST YEAR OF LIFE IN DIFFERENT SOCIAL CLASSES: RATES EXPRESSED AS PERCENTAGE OF THAT FOR ALL CLASSES TOGETHER

	0–4 wk.	4 wk. to 3 mth.	3–6 mth.	6–9 mth.	9–12 mth.	1–2 yr.
All classes	100	100	100	100	100	100
Class I ..	72	43	37	28	28	31
„ II ..	90	65	56	52	49	50
„ III ..	97	93	89	87	87	87
„ IV ..	106	108	112	113	113	108
„ V ..	108	131	143	148	151	158

Deaths occuring in the first four weeks of life are usually due to conditions peculiar to early infancy whereas those occurring in infants between four weeks and the first birthday are usually due to much the same infections as those which kill older children. Neonatal mortality (under four weeks), therefore, gives an index of the death-rates of conditions such as prematurity, birth injuries and so on, whereas the rates from four weeks to one year give an index of the behaviour of infections. This distinction is not of course absolute, but it is useful.

When death-rates from individual causes in the first year are considered it is found that on the whole death-rates from conditions peculiar to early infancy show much less increase from class I to class V than do the infections. During the second year of life measles, whooping-cough, bronchitis and pneumonia show the steepest social gradient but all the other infections examined show some variation (table 10).

In the Annual Review (Text) for 1934 the Registrar-General examined the possibility that high child mortality from measles and whooping-cough might be affected considerably by climate. He concluded that mere northerliness of situation when divorced from its accompanying increased housing density had no important effect on measles mortality and the same was broadly speaking true of whooping-cough.

The detailed study of mortality by social class is possible only for the years round about a census year and for intermediate years the less direct method of comparison between areas in which the general social conditions are known to differ markedly is often used. One of the social indices generally used is that of housing, and it may perhaps be desirable to point out here that the index of density of population per acre which was used by Farr is not of much value now, because people living in large blocks of luxury flats may be living at a higher density per acre than those living in small houses in a slum. The more usual index now is that of average number of persons per room. In the Registrar-General's Annual Review (Text) for 1937 there is an interesting comparison of mortality

TABLE 10

ENGLAND AND WALES: DEATH-RATES FROM DIFFERENT CAUSES AND IN DIFFERENT SOCIAL CLASSES IN AGE GROUP 1–2: 1930–32. RATES ARE EXPRESSED AS PERCENTAGE OF THE NATIONAL RATE. (FROM REGISTRAR-GENERAL: DECENNIAL SUPPLEMENT, 1931, p. 167)

	Measles	Whooping-cough	Influenza	Bronchitis and pneumonia	Diphtheria	Cerebro-spinal fever	Diarrhoea and enteritis	Tuberculosis of C.N.S.	Other tuberculosis
All classes (including unoccupied)	100	100	100	100	100	100	100	100	100
Class I ..	10	22	57	24	47	44	53	74	53
„ II ..	29	41	82	42					
„ III ..	80	86	93	85	89	100	83	95	88
„ IV ..	102	110	86	115	106	122	106	102	124
„ V ..	194	165	139	163	153	133	164	129	137

rates of infants at different stages of the first year of life in the years 1933–37 in certain of the county boroughs which have widely different social conditions. The comparison brings out very clearly the point made earlier that the rates of early infancy are but little affected by social conditions in comparison with those of later infancy. Stocks (1944b) has shown that between 1938 and 1942 the total infant mortality rate in Greater London has fluctuated between 43·7 in 1939 and 52·1 in 1941, whereas that of New York has shown a continuous fall from 38·3 in 1938 to 28·8 in 1942. The neonatal rates of the two great cities are not very different—Greater London 24·9 in 1942 and New York 21·0—but New York has a great advantage over Greater London in respect of its rate for infants between four weeks and one year. In 1942 that of Greater London was 21·7 and that of New York 7·8. This advantage was present before the war but is now greater than it was then.

In addition to the information on the effect of social conditions on child mortality contained in the Registrar-General's and other official reports a great deal of work has been done by individual workers.

Wright and Wright (1942) investigated the morbidity and mortality of children under five from diphtheria, measles, tuberculosis and whooping-cough in the metropolitan boroughs between 1931 and 1938, and worked out correlation coefficients between morbidity and mortality and various indices of social conditions. One of their conclusions is that, for diphtheria, morbidity is perhaps more closely associated with bad housing than is mortality and in this connexion it is interesting to recall how rare diphtheria was in the public schools investigated by the Schools Epidemics Committee (1938). Only twelve cases were reported from the public schools with an average population of over 8,000, whereas there were twenty-six cases in one of the naval schools—the subjects of Dudley's (Dudley, 1926; Dudley et al., 1934) classical investigations—with an average termly population of 881. It should be noted, however, that the boys in the naval school were on the average several years younger than boys in public schools. R. E. Smith (1935) found that of 513 boys who left Rugby between 1931 and 1935 fourteen (2·7 per cent.) had had diphtheria, 55 (11 per cent.) scarlet fever, 382 (74 per cent.) whooping-cough and 493 (96 per cent.) measles. Stocks (1942; Stocks and Karn, 1928) estimates that at least 90 per cent. of London children have a recognizable attack of measles before they are 15 but that in England and Wales as a whole the proportion is probably below 80 per cent. His estimate of the proportion of children who have had whooping-cough before age 15 is 60 per cent. for London (Stocks and Karn, 1932) and something under 40 per cent. for the country as a whole (Stocks, 1942). Among earlier papers on the influence of social conditions on morbidity and mortality from the common infections in childhood should be mentioned those of C. M. Smith (1927, 1934) and Halliday (1928) on their work in Glasgow. They concluded that the high death-rates of children from infections in the overcrowded tenements were due chiefly to high incidence and to the early age at which the children were infected.

The facts which have been given about the association between morbidity and mortality in childhood and bad social conditions are mere oases of knowledge in a desert of ignorance, and it seems doubtful if great progress can be expected until more information is available about morbidity. Perhaps this may be forthcoming in the future on the lines suggested by Stocks (1944c). It is, however, certain that social conditions are of great importance in determining mortality, and it seems probable that the total incidence of some diseases, e.g. diphtheria, is different in different classes, whereas others, e.g. measles, have a similar incidence in all classes, if children of all ages are considered, but tend to occur earlier in children living under poor home conditions. It has been shown that the differences of mortality between different classes are not nearly so noticeable in the first month of life as they are in later infancy and early childhood, facts which suggest that nurture is more important than nature in determining mortality rates in children.

Child mortality in relation to social history

'How then is the tale to be told? Into what periods shall social history be divided up? As we look back on it, we see a continuous stream of life, with gradual change perpetually taking place, but with few catastrophes. The Black Death is perhaps one, and the Industrial Revolution another. But the Industrial Revolution is spread over too many generations to be rightly regarded either as a catastrophe or as an event. It is not, like the Black Death, a fortuitous obstruction fallen across the river of life and temporarily diverting it; it is the river of life itself in the lower part of its course.' Trevelyan (1944).

The changes described in this paper are a small but not unimportant part of the changes associated with the Industrial Revolution, and it is therefore of interest to speculate on the possible relations between the trends of death-rates in childhood and the general social history of the period. First, however, it is necessary to go back further than the beginning of the statistical era (1837) because by then the Industrial Revolution was in full flood and it is impossible to assess the damage or the good caused by that flood without a brief survey of the state of affairs at its beginning.

C. Buer (1926) in her book on the early days of the Industrial Revolution points out that although the statistical data of the period 1760–1815 are imperfect it is certain that the population of England and Wales was increasing at a phenomenal rate in those years, from about six million in 1750 to about ten million in 1811, and reasonably certain that the increase was due much more to a reduction of mortality, particularly among children, than to any increase in the birth-rate. She suggests that the

main causes of this reduction in mortality were improvements in agriculture which to a large extent abolished the dangers of periodic famine, elementary improvements in housing and the sanitation of towns, improvements in medical care and the reduction in the mortality of smallpox. Farr (1885) quotes figures based on the London bills of mortality which are of interest as an indication of the reduction in child mortality which took place in London in the eighteenth and early nineteenth centuries:—

TABLE 11

TABLE: BIRTHS AND DEATHS UNDER 5 ACCORDING TO THE LONDON BILLS

Years	1730–49	1750–69	1770–89	1790–1809	1810–29
Total births ..	315,456	307,395	349,477	386,393	477,910
Deaths under 5 ..	235,087	193,694	180,058	159,571	151,794
Percentage dying under 5 ..	74·5	63·0	51·5	41·3	31·8

Farr (1885) also gives the following figures for death-rates in children for the period 1813–30 :—

TABLE 12

DEATH-RATES PER 1,000 LIVING 1813–30 AND 1841–50

	0–5		5–10		10–15	
	M	F	M	F	M	F
England and Wales ..	53·5	46·0	7·2	6·7	5·0	5·2
England and Wales, 1841–50 (table 1)	71·2	61·6	9·2	8·9	5·1	5·4

These figures, which must be accepted with reserve, are, for England and Wales as a whole, lower than those of 1841–50. Probably the early figures are an underestimate but it is likely that the death-rates of children were rising slightly in the early part of the nineteenth century because of the growth of the towns. There were, in fact, two great opposing influences at work throughout the nineteenth century. The one which tended to lower death-rates was the slow improvement in the condition of the working classes, and the other which tended to increase them was the exodus from the country where conditions were relatively favourable, to the towns where conditions were appalling. The bad conditions in towns were, however, not new. The London of Hogarth's 'Gin Lane' was not a healthier place than the London described in Simon's (1890) book and in his annual reports, but it was much smaller. This factor of rapid growth was, of course, even more important in the industrial towns. When the statistical era is considered it can still be seen that two influences are at work, for infant mortality and the death-rate 0–5 did not fall at all in the first twenty years of registration, whereas those for 5–10 and 10–15 were falling slowly (fig. 2). An influence which acted favourably and selectively on the older age groups was the slow improvement in industrial conditions and the change in the status of the child from that of wage-earner in the factory to that of future citizen in the school (Robson, 1931). Infant mortality did not really begin to fall until the beginning of the 20th century, but the rate 1–5 had been falling since 1861–70. From 1870 improvements in the sanitation of the towns were accelerated and became more effective. In the period 1900–14 the rates fell in all age groups, but the fall in the age groups 5–10 and 10–15 was arrested in the last war and the rates rose a little in the quinquennium 1916–20 chiefly because of the epidemic of influenza in 1918. The period between 1900 and the beginning of the last war was that in which the modern personal health services began. The school medical service was started in some areas in the early years of the century and was made universal in 1907. The first infant welfare centre was established in Marylebone in 1907. The public tuberculosis service began in 1911. According to Cole and Postgate (1938) real wages were rather lower in 1914 than at the beginning of the century.

Between the wars the decline of death-rates of children has been particularly rapid in the age group 1–5, and recently, from 1935 to the present time, all the rates have been falling faster than before. The inter-war period has been one of continued development of the personal health services, one of rapid reduction in the average size of families and on the whole one of increases in real wages (Cole and Postgate, 1938) and in the standard of living generally. It may be that the introduction of the sulphonamides has contributed materially to the recent declines and in the last two or three years the widespread practice of active immunization against diphtheria has been important.

The history of individual diseases

If the history of child mortality is approached from a different point of view—that of the history of individual diseases—it is found that smallpox was easily the most deadly identifiable disease of young children up to the end of the eighteenth century when it began to wane and to become more a disease of adolescents and of adults. Stevenson and Murphy (1893) give an interesting diagram, based on the London Bills, of the relative importance of smallpox, measles and whooping-cough as causes of death at all ages between 1740 and 1890. The peak year for smallpox on this diagram was 1796 when 186 of every 1,000 deaths at all ages recorded in the Bills were due to smallpox. Measles and whooping-cough caused a substantial number in epidemic years—for each disease between 30 and 50 of every 1,000 deaths recorded at all ages. These figures from the Bills are, of course, of doubtful accuracy. How far the reduction in and change in age distribution of mortality from smallpox was due to the introduction of vaccination in 1798 is a controversial problem. Greenwood (1935) is doubtful whether vaccination was sufficiently widely practised to exert an epidemiological effect and Burnet (1940), whilst conceding some influence to vaccination, considers that the natural evolution of

the disease was the most important factor. At the beginning of the statistical era scarlet fever, which had been increasing in virulence since about 1825, was already a great killing disease though it reached its peak in 1863 with a death-rate of 3,966 per million living under 15. In the 'eighties and 'nineties the mortality of scarlet fever declined rapidly, and this fact accounts to a considerable extent for the reduction in the general death-rates at ages 1–5, 5–10, 10–15 (fig. 2). The behaviour of scarlet fever, which is generally ascribed to change of type, has never been more adequately explained, and it would be interesting to re-examine the problem in the light of modern knowledge of its bacteriology. Smallpox and scarlet fever showed the most dramatic changes in the nineteenth century and the behaviour of the other important infections is sufficiently summarized in fig. 5, 6, 12, 16, 18.

With the beginning of the twentieth century an all round reduction of death-rates in childhood began, particularly of infant mortality. The mortality of bronchitis and pneumonia began to fall and the decline of tuberculosis, diphtheria and whooping-cough was accelerated. Measles death-rates did not begin to fall until the quinquennium 1916–20. The rise in tuberculosis in the last war and the influenza epidemic of 1918 interrupted the general downward tendency of the general death-rates except that of infants. Since 1918 almost every infection has shown more rapid declines of mortality than ever before except that diphtheria showed no consistent decline until recently. The declines of the mortality of measles since 1915 and of that of summer diarrhoea since 1911 have been almost as sudden and remarkable as that of scarlet fever in the 'eighties and 'nineties. Naturally the big question is whether these are changes of type which may be reversible. On the whole, the fact that declines have occurred in the mortality of other diseases—whooping-cough, bronchitis and pneumonia and tuberculosis—gives ground for hope that improvements are likely to continue provided that social conditions continue to improve. Since about 1935 the sulphonamides may have been an important influence, but it is difficult to be sure of this because streptococcal activity was falling between 1934 and 1941 (fig. 14). It is suggested that from 1915 to the present time the factor of reduction of ' family density ' has been particularly important.

Conclusions

A survey such as this of the whole field of infections in childhood over many years is a wholesome corrective to cynicism, but the great differences which still exist in different places and in different social classes are a stimulus to further research and action. It has been possible to sketch only a background for the study of social medicine in childhood and even that background has many blank spaces—notably in those parts which picture the incidence of disease rather than mortality. The study is offered in the hope that it may be of some use to those who try to solve the many problems of the prevention or cure of individual diseases.

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Figures and Tables: Sources of Figures

Fig. 1.—Census Report, 1931; R.G. Dec. Supplement, Part III, 1921; R.G. Ann. Rev. (Tables Med.), 1939.

Fig. 2.—R.G. Ann. Rev. (Tables Med.), 1940, Tab. 5; Ann. Rep. C.M.O., Min. of Health, 1933, p. 26.

Fig. 4.—Ann. Repts. C.M.O., Bd. of Education, 1929–38; Stocks (1944).

Fig. 5.—R.G. Ann. Rev. (Tables Med.), 1940, Tab. 9.

Fig. 6.—R.G. Dec. Supplement, 1921, Part III; Figures 1921–30, supplied by Dr. P. Stocks. Rates for 1938–39 calculated from R.G. Ann. Rev. (Tables Med.), Tables 1 and 21.

Fig. 7.—1911–14, R.G. Ann. Rev. (Text), Table XXXIII; 1915, calculated from R.G. Ann. Rept.; 1916–20, R.G. Ann. Revs., 1921–37. R.G. Ann. Rev. (Text), 1937, Table XXXIV; Stocks (1943).

Fig. 8.—Tuberculosis Ann. Repts. C.M.O., Bd. of Education, 1929–38. Other diseases, see under fig. 7.

Fig. 9.—Death-rates R.G. Ann. Rev. (Tables Med.), Table 9; Notification rates R.G. Ann. Rev. (Tables Med.), 1921, 1931, 1939; Table 26. Rates after 1939 from Min. of Health, Summary Repts. and R.G. Quarterly returns. Case fatality, 1911–37, R.G. Ann. Rev. (Text), 1937, Table XLII.

Fig. 10.—R.G. Weekly and Quarterly returns, 1938–44.

Fig. 11.—See under fig. 7.

Fig. 12.—See under fig. 6.

Fig. 13.—Bronchitis and pneumonia 1–5, see under fig. 7; Pneumonia and Influenza Ann. Rev. (Tables Med.) Table 7, 1921, 1929, 1939; Recent rates Summary Repts., Min. of Health and R.G. Quarterly returns (based on 1939 pop.).

Fig. 14.—See under fig. 13.

Fig. 15.—Ann. Repts. C.M.O., Bd. of Education, 1928–38. Recent figures supplied by Dr. P. Stocks.

Fig. 16.—R.G. Ann. Rev. (Text), 1935; Table I.

Fig. 17.—See under fig. 13.

Fig. 18.—Ann. Rep. C.M.O., Min. of Health, 1919–20, p. 26; R.G. Ann. Rev. (Tables Med.), 1929, 1939; Table 12.

Table 1.—R.G. Ann. Rev. (Tables Med.), 1940; Ann. Rep. C.M.O., Min. of Health, 1933, p. 26; Stocks (1943, 1944a).

Table 2.—*Inf. Mort.*, 1873–75, R.G. 39th Ann. Rept.; R.G. Ann. Rev. (Text), 1939, Table XXIII. *Later Childhood*, Ann. Rep. C.M.O., Min. of Health, 1938, p. 23; R.G. Supplement to 35th Ann. Rept.; R.G. Dec. Supp. 1921, Part III.

Table 3.—Stocks (1943).

Table 4.—Russell (1943), p. 12.

Table 5.—Med. Res. Council Special Report Series, No. 246, p. 32.

Table 6.—R.G. Quarterly Returns.

Table 7.—R.G. Supplement to 35th Ann. Rept., p. xxix.

Tables 8, 9, 10.—R.G. Decennial Supplement, 1931, Part IIA, pp. 163–167.

Table 11.—Farr (1885), p. 195.

Table 12.—Farr (1885), p. 181.

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INFANTILE DIARRHOEA

AN ANALYSIS OF 216 CASES WITH SPECIAL REFERENCE TO INSTITUTIONAL OUTBREAKS

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During a period of thirteen and a half months, from March, 1942, to April, 1943, 216 cases of diarrhoea in children under fifteen months of age were admitted to the children's isolation ward of the West Middlesex County Hospital, Isleworth. Of these cases 109 died. As this represents a case mortality which is unusually high, even for this lethal disease, an analysis of the cases was made in an attempt to assess the importance of various etiological factors and to find the actual cause of death in fatal cases. Although the main problems —the cause of the disease, and the cause of death— remain unsolved, some interesting points arose in the course of the investigation, and these are set out below. Special attention has been paid to institutional outbreaks which accounted for a high percentage of the total number of cases.

Seasonal incidence

There was no preponderance of admissions during the late summer months. Both the institutional and non-institutional admission rate tended to fluctuate, as may be seen from the graph below (fig. 1). March and February were the worst months for district cases; transfers from the maternity wards (representing the bulk of the institutional cases) were most numerous in December and April.

Although it is well recognized that the one-time heavy incidence during the late summer months no longer occurs, most workers have found some excess of admissions during the summer. Thus Campbell and Cunningham (1941) in a series of 574 cases found 52·3 per cent. were admitted between June and October; Smellie (1939) reported that in Birmingham the incidence was highest from July to October, though not markedly so, while McConkey and Couper (1938) found August to October the worst months.

The cases were all nursed in a ward consisting of thirty cubicles, with one cot to a cubicle, observing strict 'barrier' technique. The ward admitted children aged 0–12 years suffering from various infectious diseases, but cases of infantile diarrhoea usually predominated during the period in question.

Source of case

Cases were admitted throughout the year from all parts of the hospital district—a mixed urban and suburban area extending from Staines to Chiswick with a pre-war population of over 660,000. A large number, however, were transferred from other wards or other institutions, and a further series was admitted having developed symptoms within a week of discharge. Henderson (1943a) gives the incubation period of neonatal diarrhoea as two to twenty-one days; had the latter figure been adopted in classifying these cases an insignificant number would have been transferred from group 3 to group 2.

Group 1. Cases transferred from institutions, 69 (30·8 per cent.).

Group 2. Cases recently discharged from institutions, 25 (11·7 per cent.).

Group 3. No institutional history, 122 (57·5 per cent.).

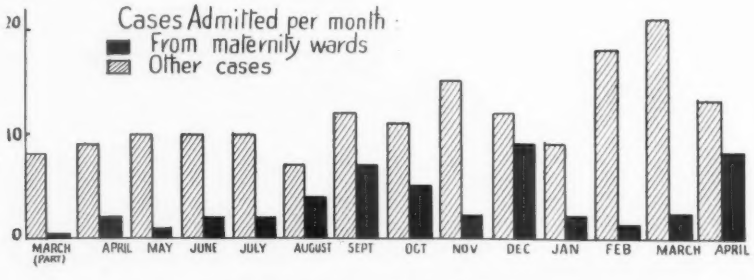

FIG. 1.—Seasonal incidence.

TABLE 1

SOURCE OF INSTITUTIONAL CASES

	Transferred	Died	Recently discharged	Died
Maternity wards ..	47	31	14	6
Infants' medical ward	12	5	3	2
Childrens' isolation ward	1	1	3	1
Other wards ..	4	1	2	0
Nursing home ..	1	1	0	0
Cottage hospital ..	0	0	1	1
Orphanages ..	2	1	0	0
Wartime day nurseries	2	0	2	1
	69	40	25	11

Some of these groups warrant further description.

Maternity cases. Explosive outbreaks of neonatal diarrhoea have recently been described by Ormiston (1941) and Sakula (1943) and the disease is often considered to be distinct from that affecting older infants. The forty-seven cases in this series which were transferred direct from the maternity wards occurred sporadically and in small groups. Following a small outbreak in December, 1942, the main maternity block, where the majority of the cases had occurred, was closed. After the block was re-opened on January 28 no further cases occurred until March 3, after which cases occurred sporadically, not only there but in an annexe in Chiswick, four miles away. The case incidence over the whole period was in the region of 3·5 per cent. [Compare Henderson (1943a and b), who found an incidence of 1·5 per cent. over a period of three years at the Simpson Maternity Pavilion, Edinburgh, and Rice et al. (1937), who, in a survey of eleven maternity homes in New York over a period of three years found an average case incidence of 14 per cent.] There was never a time when practically every infant at risk was affected, as in Sakula's series.

There was nothing to distinguish these cases from others in the same age group. There were altogether seventy-one cases aged under one month with forty-eight deaths (67·6 per cent.); of the forty-seven maternity cases thirty-one died (66 per cent.). The history, course and complications were as varied in all these tiny infants as they were in the older patients, and post-mortem findings were similar. For instance, in twenty-six out of forty-seven post-mortem examinations on infants of all ages there were signs of middle ear suppuration (55 per cent.), and in eight out of fifteen ' neonatal ' cases (53 per cent.).

FEEDING HISTORY. Among the sixty-one cases transferred or re-admitted after discharge from the maternity wards not one had been wholly breast fed. One very mild case, who made a rapid recovery, was breast fed on admission to the children's ward, but had had complementary feeds before transfer. Three premature infants were having expressed breast milk intranasally or from a bottle; seven infants were partially breast fed at the onset of the disease; the remaining fifty were wholly artificially fed.

MATURITY. Ten infants were premature (weighing 3 lb. 2 oz. to 5 lb. 4 oz. at birth) and of these eight died.

Cases from the infants' medical ward. This ward supplied an occasional case of diarrhoea. After a long period of freedom from diarrhoeal conditions five cases occurred within forty-eight hours; two died and the rest were very ill for a long time. This was the only outbreak affecting several cases at once in this ward during the period in question; it followed, and may have been attributable to, the arrival of a new nurse on the ward with a severe cold.

Cases from the isolation ward itself. One case of diarrhoea occurred in an infant admitted for a non-diarrhoeal infection—in a boy aged fourteen months who developed fatal diarrhoea ten days after having been admitted with whooping cough. Three cases were re-admitted shortly after discharge from the ward, their former admissions having been for some other infection, and one of these cases died.

Relapses and re-infections. In a disease where no specific pathogen has been isolated it is often impossible to distinguish between relapses and re-infections. In forty-six cases a sudden relapse occurred; twenty-nine died. In fourteen of these cases, of whom ten died, the relapse occurred when the infant seemed to be improving; four were definitely convalescent; the remaining cases were already very ill when the relapse occurred.

Mortality

As in other series the death rate falls with increasing age, and is highest in the dehydrated cases.

TABLE 2

MORTALITY BY AGE AND DEHYDRATION

Age in months	Cases	Died	Percentage died	Dehydrated on admission	Dehydrated per cent.
0– 1	71	48	67	40	56
1– 3	50	26	52	23	46
3– 6	52	21	40	23	44
6– 9	18	6	33	8	44
9–12	11	5	45	5	45
12–15	10	3	30	3	30
	215	109	51	102	45

Dehydrated on admission, died 71 (70 per cent.)
Not dehydrated on admission, died 38/114 (33 per cent.)

Although it is difficult to compare mortality rates in a disease in which objective standards of severity are lacking, it is clear that the death rates quoted above are unusually high. The total mortality in this series (51 per cent.) approximates to that among Campbell and Cunningham's dehydrated cases. Indeed, the difference in mortality between dehydrated and non-dehydrated cases and between different age groups is much less than in their series

—their non-dehydrated cases had a mortality of only 2·7 per cent. Other series quoted by Cohen, Miller and Kramer (1933) vary from 14 to 88 per cent. mortality. Field, MacCarthy and Wyllie (1943) among a hundred cases, of whom seventy-eight were dehydrated, had only twenty-three deaths, but they do not state whether the series included any very young infants. It may be noted that, of the thirty-eight fatal cases in this series not dehydrated on admission, nineteen were under one month of age. Of one hundred and fourteen cases not dehydrated at the onset forty-four later became so, and twenty-two died. Sixteen died without showing dehydration at any time.

Etiology

This subject will be considered under four headings—history, clinical findings, pathology and results of treatment, each of which throws some light on the question.

History

(i) FEEDS. The outstanding feature in the feeding history of these infants is the frequency of early weaning.

TABLE 3

FEEDING HISTORY

	Cases	Percentage of Cases	Died	Percentage died
1. Breast fed for six months or more or at onset of disease	15	7	5	33
2. Artificially fed ..	201	93	104	52
i. Breast fed for less than one month	131	60·7	80	61
(*a*) cases aged under one month ..	71	32·8	47	66·2
(*b*) cases aged over one month	60	27·7	33	55
ii. Breast fed for over one month	39	24·3	11	28
iii. Date of weaning not recorded	33	15	13	40

The fact that 60·7 per cent. were weaned before reaching the age of one month is noteworthy. Even a few weeks breast feeding appears to offer some protection against this disease. Thus the mortality among those weaned under one month was 61 per cent. as compared with 28 per cent. among those breast fed for a month or longer. Similar figures (76·6 per cent. and 25·9 per cent.) are given by Smellie, derived from a series of five hundred cases of whom 59 per cent. had been breast fed for less than a month.

REASONS FOR WEANING. In three cases this was due to maternal illness, in four to medical advice, in two to having to go out to work, and in a few to local conditions of the breast. The overwhelming majority, however, gave up because lactation failed. By far the commonest story was ' When I got up, the milk went.'

TYPE OF BOTTLE FEED. Twenty-one out of two hundred and one bottle-fed patients were receiving cow's milk mixtures. All the others were fed on dried or condensed milk, which is evidence against an ordinary milk-borne infection. All the popular brands of infants' foods were well represented, there being little to choose between them in this respect.

The overwhelming preponderance of bottle-fed infants in all published series of cases of infantile diarrhoea is perhaps the most notable feature of this disease, but its exact etiological significance is less clear. It can be argued that either the milk or the bottle is the vehicle of a pathogenic organism or virus, or that artificial feeding irritates the bowel and makes it less resistant to bacterial invasion (enteral infection) or toxins (parenteral infection); antibodies in human milk have also been postulated. However, in this last case, one would expect an equal protection to be offered to the breast-fed infant against other infections, and although there is a considerable amount of evidence that breast-fed babies are less liable than are bottle-fed infants to such diseases (e.g. Ebbs and Mulligan, 1942; Deeney and Murdock, 1944), it is not found that they are practically confined to the bottle fed as in infantile diarrhoea.

(ii) PRESENTING SYMPTOMS. In eighteen cases this was stated to be a ' cold,' and in seventeen cases loss of weight was first noticed. In the remaining cases the earliest symptoms were diarrhoea, vomiting or loss of appetite. The seventeen cases showing early loss of weight were mostly institutional cases; were babies normally weighed daily this presenting symptom might prove to be much commoner, and suggests some disturbance outside the alimentary tract.

Clinical findings

Seventy-five cases (34·7 per cent.) showed clinical signs of parenteral infection on admission.

TABLE 4

PARENTERAL INFECTIONS ON ADMISSION

	Cases	Died
Otitis media	21	8
Bronchitis or pneumonia ..	25	17
Septic skin lesions	21	11
Upper respiratory tract ..	5	1
Thrush	3	3
	75	40 (53·3 per cent.)

Too much weight must not be attached to such findings in the absence of a control series of infants admitted with other diseases. Furthermore, the high percentage of extremely small infants made accurate diagnosis exceptionally difficult, and in nineteen cases post-mortem evidence was found of an infection undiagnosed during life. It is interesting that the mortality among these cases is almost identical with that of the whole series (51 per cent.).

Bacteriology and pathology. In the few cases where the stools were fully examined no pathogenic organisms were found—even in three infants whose

stools contained blood or mucus, and notwithstanding the fact that several cases of Sonne dysentery were nursed in the ward during this period.

TABLE 5

POST-MORTEM FINDINGS

Otitis media	12	34 (70 per cent.)
Mastoiditis	4	
Bronchopneumonia	8	
Otitis and pneumonia	10	
Cranial sinus thrombosis (without ear disease)	3	
Intestinal haemorrhage	1	
Intestinal exudate	2	
Various	7	
	47	

Whatever may be the etiological significance of the various parenteral infections noted above, the absence of any signs of inflammation of the gut in all but three cases is noteworthy and is typical of this disease. The part played by infections such as otitis media in the causation of infantile diarrhoea has been the subject of much controversy.

Thus Marriott and Hartman (1933) stated that one hundred and sixty-six out of two hundred cases had signs of disease in the ear or throat on admission, and even more after the initial dehydration has been treated. Maizels and Smith (1934) found post-mortem evidence of otitis media in forty-one out of sixty-eight fatal cases of ' D and V,' in only ten out of thirty-three other cases. On the other hand, Findlay (1932) points to the differing seasonal incidence of otitis media and diarrhoea (though that would not apply to the present series) and the different breast-feeding rate in cases of diarrhoea and pneumococcal otitis with meningitis (9 per cent. and 44 per cent. respectively). He did routine myringotomies on all cases of diarrhoea in one ward and none in another without affecting the results, and finally reports seven deaths in nine cases on whom bilateral mastoidectomy was performed—in five cases on not very ill babies. Wishart (1930) reports an exhaustively investigated series of one hundred and sixty-eight cases of infantile diarrhoea. He found the bacterial flora of the upper respiratory tract and ears the same in his cases and in the controls; fifty-seven had infections on admission, and one hundred and five developed such infections in hospital. Twelve out of thirteen patients subjected to mastoidectomy died. He points out that in a series of one hundred and thirty-three patients under two years of age on whom mastoidectomies were performed, diarrhoea, vomiting or loss of weight were present in only eighteen cases, constipation being frequently present in the remainder. Smellie (1939), who found evidence of parenteral infection in 46·2 per cent. of admissions for infantile diarrhoea, also points to the differing seasonal evidence in the two conditions. Others (Cooper, 1937; Campbell and Cunningham, 1941) report various parenteral infection rates (40·7 per cent. and 30·5 per cent. respectively), but do not state categorically whether or not they regard these infections as the cause of diarrhoea. It seems unlikely, taking other factors into consideration, that otitis media or any other parenteral infection can be considered *the* cause of the diarrhoea, even when present, though it may be a contributory or precipitating factor.

In the voluminous literature, however, adequately controlled series which enable a comparison of the incidence of otitis media in diarrhoeal and in non-diarrhoeal diseases of infancy are seldom found. Finally, the comparative infrequency of diarrhoea as a dangerous complication of severe cases of frank parenteral infection must be noted (e.g. Wishart, 1930; Stirk Adams, 1937). In the present series only two infants would have been dangerously ill without their diarrhoea—a case of lung abscess in which the diarrhoea was a terminal condition, and a severe case of septic burns in whom it responded as rapidly as did the burns to treatment with propamidine jelly.

Results of treatment. If infantile diarrhoea were solely attributable to parenteral infection treatment of the latter should be an effective way of treating the diarrhoea. In this series cases of otitis, bronchitis and pneumonia, and many cases with unexplained pyrexia were treated with full doses of sulphapyridine or sulphadiazine, by mouth or intravenously. Fifty-six cases were so treated and twenty-eight died (50 per cent.)—again no improvement on the general mortality (51 per cent.). Myringotomy was performed when required, but did not appear to affect the result as far as the diarrhoea was concerned.

In March, 1943, sulphasuxidine, a non-absorbed sulphonamide the action of which is to sterilize the gut, first became available. Sixteen cases were treated with courses of 1·5 to 3 grammes per day for one week, and three died. Of seven dehydrated cases so treated none died. Eight treated cases were passing the dreaded orange stools, and of these two died, compared with thirty out of thirty-six untreated cases with this symptom. Two of the treated cases who recovered were so desperately ill as to be described as ' moribund on admission ' in the case records.

The success of sulphasuxidine in this very small group is interesting, and it is to be hoped that the results of treatment in larger series will be published. Similar results are reported by Twyman and Horton (1943) in a series of twenty-two cases of neonatal diarrhoea. Henderson (1943) obtained striking improvement in the results of treatment of neonatal diarrhoea following the introduction of sulphaguanidine. Should the non-absorbed sulphonamides be definitely proved superior to those of the sulphapyridine series in the treatment of infantile diarrhoea the fact would be of definite etiological significance, and should help to determine the relative importance of enteral and parenteral infections in this disease.

Course and complications

No attempt will here be made to describe the all too familiar course of the typical fulminating ' D and V,' showing on admission the depressed fontanelle, inelastic skin, greyish pallor, unnaturally red lips and sunken, rapidly glazing eyes. There were fourteen such infants who died within a few hours of admission, and many others whose death was merely postponed a few days by intravenous

'drips' which corrected the dehydration but could not cure the disease. Instead, some account will be given of the still larger group (in this series), in which the infant, who was either not dehydrated on admission, or in which water balance had already been successfully corrected, had a relapse, generally became dehydrated, and all too frequently died.

There is a large, well-marked group of cases who on admission are pale and hollow-eyed, but not dehydrated, and have from the start severe and intractable diarrhoea. Frequent, offensive, watery green or orange stools are passed, but vomiting is either absent or responds to twenty-four to forty-eight hours' starvation. Some slight progress may be made, but such notes as 'not dehydrated—but still pale and hollow-eyed' or 'still ghastly diarrhoea' reappear with surprising frequency in the case records. Then after a period which may be as long as two or three weeks, a relapse occurs. The temperature rises, diarrhoea becomes, if possible, worse; the infant refuses his feeds and may even vomit and become slightly dehydrated. Mouth feeds are discontinued, an intravenous drip is set up, and within a few hours the dehydration is relieved. Nevertheless watery, offensive stools continue to pour from the child, and soon the dreaded 'coffee ground' vomitus appears, an almost infallible herald of death.

Perhaps an even more distressing type of case is seen in the infant who, not desperately ill on admission, or at any rate apparently on the road to recovery, suffers such a relapse and dies. It is this type of case which gives rise to the suspicion of reinfection in the ward, leading to a constant overhauling of the barrier-nursing technique, a repeated scrutiny of the therapeutic measures adopted. As long as the etiological agent is unknown, it can never be proved whether or not such cases represent reinfections or relapses. Suspecting reinfection led to the discharge of infants at the first possible moment, yet even so the average stay in the ward of recovered cases was 43·1 days, and in twenty-two cases was over two months—a measure of the severity of this illness in young infants.

There are four symptoms of grave if not fatal import—orange stools, blood-stained or 'coffee grounds' vomitus, jaundice and hyperpyrexia.

ORANGE STOOLS occurred in forty-four cases with twelve recoveries.

'COFFEE GROUND' VOMITUS was noted in twenty-six cases, with but one recovery. Such vomiting is usually an agonal symptom, but in a few cases it was the first sign that the illness was likely to be fatal.

JAUNDICE is especially common in young and premature infants, in whom it was frequently seen unaccompanied by dehydration. Of twenty-three jaundiced cases, one was taken home against advice and could not be traced—all the others died.

HYPERPYREXIA is a common terminal event. As noted above, a rise of temperature frequently heralds a relapse, especially if it is accompanied by marked lassitude and irritability. Just before death a temperature of 106° to 107° F. is not uncommon. A curious case was that of a tiny infant of twenty-six days whose temperature swung between 95° and 107° F. for ten days, without any signs beyond the usual dehydration and orange stools, but who made a complete recovery after a course of sulphapyridine.

Parenteral infections occurring during the course of the disease

Twenty-six such cases occurred—otitis media (11), bronchitis and pneumonia (4), skin lesions (2). Nine of these cases died. Two case histories serve to illustrate some of these points.

Case 131. Male infant aged nine days. Transferred from maternity ward where diarrhoea had been noted for one day. Never breast fed. On dried milk.

ON ADMISSION. Pale, not dehydrated, no abnormal signs, severe diarrhoea, occasional vomiting. Slight improvement but stools frequent and offensive till the fifteenth day, when vomiting and slight dehydration were noted. All feeds by mouth were stopped and an intravenous drip set up and continued for three days, during which there was marked improvement. Next day copious vomiting and frequent watery stools occurred. Fluids were administered by means of a gastric drip for two days, when another intravenous drip was set up and continued for two days. Two cyanotic attacks followed and the child was put in an oxygen tent. Some improvement was noted until the twenty-fifth day, when once more dehydration reappeared. A third intravenous drip was set up and continued until the child's death on the twenty-ninth day.

POST MORTEM. R. mastoiditis, bronchiolitis.

Case 206. Male infant aged three months. Breast fed three weeks: on dried milk. Cough and running eyes three days.

ON ADMISSION. Cyanosed but not dehydrated. Signs of right basal pneumonia. Offensive stools. He was given a course of sulphapyridine (6·5 gm. in 5 days). By the fourth day the temperature was normal and the chest clear. The general condition was very poor and the diarrhoea became worse. Fifth day, temperature 100° F., offensive stools. Tenth day, slight improvement. Sixteenth day, temperature 100° F., reluctant with feeds. Pale, not dehydrated. Left drum injected. Eighteenth day, pale, hollow-eyed, offensive stools. Ears and chest clear. Twenty-fourth day, diarrhoea slightly better. Thirtieth day, severe diarrhoea, very slight dehydration, no vomiting. Took saline well by mouth. 3.30 a.m. Vomited. Intravenous drip set up. Thirty-second day, not dehydrated, no vomiting, took 2 oz. saline hourly, drip discontinued. Thirty-third day, died.

Treatment

The routine treatment of these infants consisted of early starvation, graduated feeds, correction of water balance according to a schedule (based on that of Arnott and Young, 1942), and blood transfusion once the acute stage was over. In all but the mildest cases of dehydration fluid was administered by means of an intravenous drip. This could be relied upon to correct dehydration, but only too frequently failed to save life. Drug treatment has been described above.

Discussion

The results of the analysis of this series of cases throws little new light on the etiology of infantile diarrhoea or on the actual cause of death in fatal cases. The high incidence of post-mortem evidence of parenteral infection is suggestive, but the association cannot be proved to be causal. The high incidence during the winter months, the cases in which illness appeared to start as a 'cold' and the small ward outbreak following exposure to adult coryza lead to the suspicion of the upper respiratory tract as the portal of entry of the infection. The absence of pathological or bacteriological evidence of intestinal infection and the frequency of loss of weight as a presenting symptom make it at least seem likely that the cause of the illness lies outside the bowel. On the other hand the uniquely high incidence of artificial feeding in this disease, and the success (should this be confirmed) of the non-absorbed sulphonamides in treatment lead to opposite conclusions. It seems unlikely that infantile diarrhoea is a disease that can be attributed to a single cause. Many factors appear to be involved, and when several act together on an infant of the susceptible age group the result seems to be diarrhoea of a severity that treatment is only too often powerless to mitigate, whether that treatment be aimed at curing parenteral infection or correcting water balance.

When epidemiology is considered, this series emphasizes the danger inherent in infant communities, whether in maternity homes, hospitals or nurseries. Forty infants died of diarrhoea contracted in an institution, or fifty-one if 'recently discharged' cases are included.

The remaining one hundred and twelve cases, of whom fifty-eight died, were admitted from the hospital district over a period of just over a year. This points to a high incidence of a highly fatal type of diarrhoea in an area which is largely 'residential' in character and by no means poverty stricken. Elsewhere (Gairdner, 1944) it has been shown that Greater London, including the residential suburbs, has a diarrhoeal mortality out of all proportion to its total infant mortality, and that, whereas the diarrhoeal mortality of the aggregate of county boroughs has shown a more or less steady decline since 1921 that of London has tended to rise since 1928 and, since 1930, has been consistently above the county borough rate (fig. 2).

Why the mortality from infantile diarrhoea should be stationary or increasing in an area where other causes of infant death are not ill controlled (the infant mortality in the outer ring of Greater London is among the lowest in the country) it is difficult to see. Two incontrovertible facts stand out from the confusion concerning the etiology of this disease—its high incidence among bottle-fed and among institutional infants. There does not appear to be any evidence that breast feeding has declined more rapidly in London than in the country as a whole (Gordon, 1942; Robinson, 1942). Are London infants sent into hospital and other institutions more frequently than elsewhere? If this is so, and if this is the cause of the deplorably high incidence of one of the most fatal diseases of infancy in our capital, it should cause even greater reluctance than already exists in many quarters to sending infants into institutions, unless the latter are fully equipped with sufficient isolation accommodation to prevent such outbreaks.

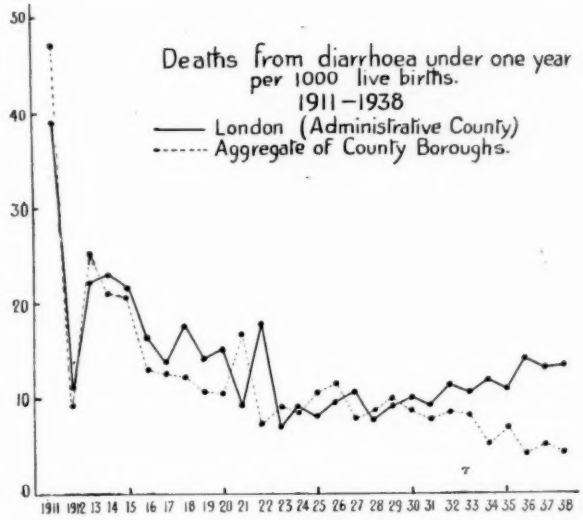

FIG. 2.

Thanks are due to Dr. J. B. Cook, Medical Director of the West Middlesex County Hospital, for permission to publish these cases, and to Professor J. Ryle, Dr. J. O. F. Davies and Dr. P. Holman for their helpful advice and suggestions.

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THE RESULTS OF ROUTINE PROPHYLAXIS AND TREATMENT OF RICKETS IN WAR-TIME NURSERIES

BY

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In an earlier paper (Krestin, 1944) it was shown that rickets, although generally of a mild nature, still presented a problem in infant entrants to the war-time nurseries of Preston, since 36 per cent. of those under two years were found to have evidence of past or active disease, and in some of the poorer districts the incidence was considerably higher. Moreover, it was further noted that even when mothers had previously availed themselves of the free distribution of the Ministry of Food cod-liver oil for their babies, the results were still disappointing. Similarly, in a recent widespread survey throughout Great Britain and Ireland published by the Ministry of Health (1944) 73 per cent. of infants with x-ray evidence of rickets were said to have previously received cod-liver oil or other vitamin D preparation. Since the efficacy of cod-liver oil both in the prophylaxis and the treatment of this disease is now beyond doubt, it is clear that such results could be due only to inadequate dosage or to carelessness and irregularity of administration. It seemed, therefore, of interest to assess the results of the prophylactic use of cod-liver oil and of the therapeutic use both of this and of a more concentrated preparation of vitamin D for active rickets, as used in the routine of the Preston war-time nurseries where the doses and regularity of administration could be assured.

The subjects of this investigation were all unselected infants and children admitted to three residential and ten day nurseries. All were full-term babies. The conditions and diets were fairly uniform and constant in all the nurseries. Infants under six months were fed on a dried or fresh cow's milk. All were examined clinically soon after admission, whilst all under three years and some older children had x-ray films taken of the distal ulna epiphyses. Thereafter, regular clinical examinations were carried out at monthly or shorter intervals. All were again x-rayed at the end of six months, and the 'controls' with a small number of the others were x-rayed at shorter intervals during this period. More frequent x-ray examinations were not possible owing to the distance of the nurseries from the x-ray centre. Chemical investigations of the blood were not practicable.

Three groups were studied, a ' control,' a ' prophylactic ' and a ' therapeutic.' The first two were free from all obvious disease or defect on admission, and the third from all disease other than active rickets as determined radiologically.

The cod-liver oil used was that supplied by the Ministry of Food and was ' fortified ' by the addition of calciferol (D_2) so that one drachm contained 700–800 I.U. of vitamin D. It was given in the pure form in a teaspoon in two divided doses after meals. In the case of infants under six months the initial dose was half a drachm twice daily and this was increased within a week to the full dose stated in table 1. In about 2 or 3 per cent. the oil could not be given owing to refusal on the part of the child, the appearance of skin rashes, or gastro-intestinal upsets. These were then given a more concentrated preparation of vitamin D, but are not included in this paper. Those in day nurseries received the doses on six days, and the residents on seven days a week. The concentrated preparation used in some of the ' therapeutic ' group was given in a single daily dose and contained 2000 I.U. of vitamin D per c.c.

The observations of the ' control ' group were made during a six-months' period from the autumn of 1943 to the early spring of 1944. Those of the other two groups were made during this period as well as the same period of the previous year. The diets and conditions in the nurseries during these two periods were similar and the climatic conditions much the same. Further, no other method of treatment, such as ultra-violet radiation, was used in these children.

Discussion of results

Control and prophylactic groups—table 1. In these groups the development of rickets was recognized either by the x-ray changes or by the clinical signs. The x-ray manifestations will be considered below, but it should be stated that in early or mild cases no abnormal changes may appear in the lower ulna epiphyses, or they may last for so short a time that they may be missed unless films are taken regularly at brief intervals. After the third month and before the sixth month craniotabes, i.e. areas of asymmetrical softening of the cranial bones limited to the region of the lambdoid suture, was found to be a reliable sign of the disease. After the fourth or fifth month, a well-developed enlargement of the costo-chondral junction of the fifth to the tenth ribs

TABLE 1

THE PROPHYLAXIS OF RICKETS BY ROUTINE COD-LIVER OIL

Age group	Controls			Received cod-liver oil											
				1 drachm (700–800 I.U. Vit. D)			2 drachms (approx. 1500 I.U. Vit. D)			3 drachms (approx. 2100 I.U. Vit. D)			4 drachms (approx. 3000 I.U. Vit. D)		
	Number Examined	Developed Rickets	Remained Free	Number Examined	Developed Rickets	Remained Free	Number Examined	Developed Rickets	Remained Free	Number Examined	Developed Rickets	Remained Free	Number Examined	Developed Rickets	Remained Free
0 to 6 months	44	30 (68 per cent.) (23 x-ray positive)	14	18	12	6	28	3 (10·7 per cent.)	25	—	—	—	—	—	—
6 months to 1 year.				—	—	—	28	2 (7 per cent.)	26	15	0	15	—	—	—
1 to 2 years ..	28	3 (10·7 per cent.)	25	—	—	—	55	6 (10·9 per cent.)	49	11	1	10	44	0	44
2 to 3 years ..	15	0	15	—	—	—	63	0	63	—	—	—	60	0	60
3 to 5 years ..	20	0	20	—	—	—	70	0	70	—	—	—	56	0	56

The diagnosis of rickets was based on x-ray and/or clinical signs.

was accepted as diagnostic in those children in whom scurvy had been previously eliminated. Moreover, this latter manifestation may persist for weeks or months after the skiagraphic appearances return to normal. Isolated signs, such as delayed closing of the fontanelles, frontal cranial bossing, and bowing of the legs were found to be unreliable criteria. It is hoped to consider the diagnostic value of these signs more fully elsewhere.

A. CONTROL GROUP. These received no vitamin D preparation throughout the six months' period of observation if signs of rickets did not appear, otherwise treatment was started immediately after the appearance of such signs. In all other respects the diets and conditions under which they lived were the same as for those of the other two groups.

It will be seen that in those under one year, thirty of the forty-four (68 per cent.) developed manifestations of rickets, twenty-three of them showing positive x-ray changes, and seven clinical signs only.

With the object of determining whether the nature of the diet or the administration of vitamin D before admission had any influence on these results, a comparison of these data together with the age at the beginning of the investigation is given for the 0–1-year group in table 2.

No importance can be attached to such small figures. Previous vitamin D administration appears to have had a favourable influence, but age seems to be of most significance in this series, since twelve of the fourteen who remained free were six months or older on admission.

In those between one and two years of age, the drop to 10·7 per cent. in the development of rickets is striking. Schmorl (1909) in his extensive histological study found a considerable reduction in the numbers affected during the second year. Two possible factors may be mentioned in this connection. First, there is the rate of growth with which the development of rickets is closely related. This is

TABLE 2

AGE, TYPE OF FEEDING AND ADMINISTRATION OF VITAMIN D BEFORE ADMISSION TO NURSERIES IN CONTROLS UNDER 12 MONTHS

	Under 6 months	Over 6 months	Number exam.	Breast fed	Bottle fed	Number exam.	Previous Vit. D	No Vit. D	Number exam.
Developed rickets	12	18 (60 per cent.)	30	11	19	30	12 (40 per cent.)	18	30
Remained free ..	2	12 (86 per cent.)	14	4	10	14	8 (57 per cent.)	6	14

rapid during the first twelve months, but slows down considerably during the second year. Second, the change of diet during this period may be of some significance. Up to the fourth month this, in the nurseries, consists of either dried or fresh cows milk, which, according to values given by Fixsen and Roscoe (1937–38, 1939–40), probably contains less than 2 I.U. of vitamin D per 100 gm., so that the total daily intake is probably less than 10 to 12 I.U. From the fifth month onwards small additions are made in the process of weaning, and after the twelfth month the child receives a mixed diet including butter, vitaminized margarine, egg yolk and fish. On the basis of the same values a child in its second year will probably receive from 20 to 25 I.U. daily from the food at the nurseries. This, though very much less than the minimum daily requirements of 300 I.U. suggested by Bicknell and Prescott (1942) may however, be sufficient to protect a child, who, for whatever the reason, was able to avoid the disease up to the end of the first year.

Of the children who had reached two years or more at the beginning of the enquiry, none developed rickets.

B. PROPHYLACTIC GROUP. During a preliminary observation period a small series of infants under six months were given 1 drachm (700–800 I.U.) of cod-liver oil daily. Of these, two-thirds developed rickets. After this period 2 drachms, i.e. approx. 1500 I.U. was given to this age group, of whom three out of twenty-eight (10·7 per cent.) developed rickets. Those over six months but not yet twelve months were divided into two series, one receiving 2 drachms (1500 I.U.) and the other 3 drachms (approx. 2100 I.U.) daily. Of twenty-eight of the former, 2 (7 per cent.) developed signs, but all fifteen of the latter group remained free. Thus it would seem that although the equivalent of a daily dose of 1500 I.U. will protect most infants under one year, it is probably safer to give not less than 2000 I.U. This is double the minimum daily dose recommended by Park (1940), and considerably more than the doses suggested by most authorities, including Jeans and Stearns (1935), Mackay (1942) and Bicknell and Prescott (1942).

Children between one and two years were divided into three sub-groups receiving two, three and four drachms daily. Of those receiving four drachms (approx. 3000 I.U.) all remained free; one of the four receiving three drachms developed rickets and six, i.e. 10·9 per cent. of the fifty-five receiving two drachms developed signs of the disorder. The last figure is surprisingly high compared with the controls developing rickets in the same age group, and although the numbers concerned are too small to be of much significance, they suggest that whilst the liability to rickets is not great at this age, those who are liable may require higher doses than during the first year.

As would be expected from the control series, all over 2 years remained free from disease on the doses given.

2. Treatment of rickets—table 3. Although experience in these nurseries has shown that craniotabes as defined above may be accepted as reliable evidence of active rickets in infants over three months, the disappearance of this sign at about the sixth month does not constitute proof that healing has occurred. Enlargement of the costo-chondral junctions, the only other reliable clinical sign in infancy, can, however, persist for weeks or even months after activity has ceased. Hence, even though the experienced examiner can often make a correct guess by the firmer and more sharply defined feel of these enlargements that the condition is healed, the only certain means of deciding this matter, in the absence of bio-chemical investigations, is by the radiological examination of the ulna epiphyses. Thus, the diagnosis and the results of treatment referred to in table 3 are all based on x-ray films.

The radiological appearances of active and healing rickets have been fully and clearly described by Wimberger (1923), Hess (1930), and others, and so require no detailed description here. The cases under present consideration are divided into two series: (a) 'mild,' recognized by a fluffiness and fraying of the metaphyses; and (b) 'more severe,' in which these changes were more advanced and accompanied by the typical cupping and broadening of this zone. Healing was recognized by the

TABLE 3

TREATMENT OF RADIOLOGICALLY ACTIVE RICKETS BY COD-LIVER OIL AND A CONCENTRATED VITAMIN D PREPARATION

Age group	'Mild' activity; cod-liver oil									'More severe' activity		
	2 drachms (1500 I.U.)			3 drachms (2100 I.U.)			4 drachms (3000 I.U.)			3250 I.U.		
	Number treated	Not healed	Healed	Number treated	Not healed	Healed	Number treated	Not healed	Healed	Number treated	Not healed	Healed
0 to 6 months	15	0	15	—	—	—	—	—	—	12	0	12
6 months to 1 year.	17	0	17	—	—	—	—	—	—	11	0	11
1 to 2 years ..	—	—	—	5	1	4	4	0	4	16	0	16
2 to 3 years ..	—	—	—	3	0	3	2	0	2	5	0	5

appearance of a fresh zone of provisional calcification just distal to the old frayed or fluffy one, which became thicker and more sharply defined as the process became more consolidated. Six months after the beginning of treatment most of the radiographs appeared normal. Although in some of the initial films it was not always possible to decide whether healing had actually started, subsequent x-rays always settled this doubt. It should be emphasized that in none of the cases here discussed were there signs of advanced clinical disease, such as gross deformity of the chest or bending of the bones.

Those showing ' mild ' activity were treated with cod-liver oil. During a preliminary trial period a small number in each of the age groups up to three years received 1 drachm (700–800 I.U.) daily, but a high proportion failed to show healing. Thereafter, the daily doses given were as shown in table 3.

It will be seen that 2 drachms or about 1500 I.U. was sufficient for all those under twelve months. In the one to two year age group one child failed to heal on 3 drachms (2100 I.U.), but the others in this small group and the very small numbers in the two to three year group all healed on 3 and 4 drachms (i.e. 3000 I.U.). Thus in infants under two years there appears to be little difference between the amount of vitamin required for protection and that required for healing a mild or early degree of active rickets.

The ' more severe ' series all received a standard dose of 3250 I.U. given as a concentrated preparation containing 2000 I.U. per c.c. This was followed by healing in all cases.

It may be mentioned that children showing active disease in the third year all had a rather long history, which suggested that the condition almost certainly began before the age of two years.

Although this article is primarily concerned with full-term and otherwise healthy infants, it may be relevant to stress here the well recognized fact that prematurity and other circumstances may require doses of vitamin D considerably greater than those discussed above. Thus infants recovering from acute illness or marasmus and so growing relatively fast, and infants receiving thyroid require doses approximately double those given above. Two premature infants under six months both developed rickets on the maximum amount of cod-liver oil it was found possible to administer daily, i.e. 3 drachms (2100 I.U.). Park (1940) considers that such infants require from 5000 to 10,000 I.U. of vitamin D daily, and also draws attention to the danger of lipoid pneumonia following aspiration when large doses of oil are given to feeble infants or those liable to vomiting.

Summary and conclusions

(1) The results of the routine administration of the Ministry of Food cod-liver oil containing 600–800 I.U. of vitamin D to the drachm, for the protection against rickets, and of this oil and a more concentrated preparation of vitamin D for infants showing radiologically active disease, as used in the Preston war-time nurseries are discussed.

(2) The diagnostic criteria by which the development of the disease was recognized and the manifestations of activity are briefly considered.

(3) In a series of controls under twelve months receiving no protective vitamin, two-thirds developed rickets, whereas in a similar series between one and two years only 10·7 per cent. developed the disorder. Control children over two years all remained free during the six months period of observation.

(4) A daily dose of one drachm of cod-liver oil (600–800 I.U.) failed to protect two-thirds of infants under six months. Two drachms (1500 I.U.) protected most and 3 drachms (2100 I.U.) all the infants under one year. About 11 per cent. of infants between one and two years receiving 2 drachms daily developed rickets, but all remained free on 4 drachms (3000 I.U.).

(5) Infants under one year showing ' mildly ' active rickets were all cured on 2 drachms (1500 I.U.) of cod-liver oil a day. Those between one and three years appeared to require doses up to 3000 I.U.

All the infants showing a ' more severe ' degree of activity responded well to daily doses of 3250 I.U. given as a concentrated preparation.

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RENAL DWARFISM

A RECORD OF ABNORMALITIES IN CARBOHYDRATE METABOLISM

BY

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Abnormalities have been observed in the carbohydrate metabolism of three of the four cases of renal dwarfism summarized below. Since the abnormalities do not appear to have been noted in previous cases of renal dwarfism it is felt that a brief record of the findings is of interest.

Case summaries

(Only relevant points are recorded)

Case 1. Male, aged 8 years when first seen. Birth weight, 7 lb. Difficult labour lasting three days. Growth had been stunted since the age of 3 years. Thirst and polyuria were noted by the mother at the age of 4 years. When first examined (January, 1942) he showed height, 42 inches; weight, 38 lb. He was healthy and intelligent in appearance. The limb–trunk ratio was normal. Blood pressure was 110/70 mm. Hg. The clinical examination was negative. The urine was pale, specific gravity 1002 to 1010, and contained no abnormal constituents. The twenty-four-hour volume was 60 to 110 oz. The x-ray of skull showed an unusually massive dorsum sellae and posterior clinoid processes. An excretion urogram (14 c.c. of uropac) showed no dye in pelves, ureters or bladder. Active rickets (type A) was first noted radiologically in November, 1942. The urine was tested daily from January to May, 1942, and for short periods on several subsequent occasions. No albumin found apart from a trace on two occasions. When last seen in November, 1943, however, the urine contained a cloud of albumin and the blood pressure was 155/120 mm. Hg (the first abnormal reading noted). Walking had deteriorated and the rickets had become more severe. He died in March, 1944: no details of death were available.

BLOOD CHEMISTRY
(mgm. per cent.)

Date	Blood urea	Blood creatinin	Serum phosphorus	Serum calcium
April, 1942 ..	52	—	—	—
May, 1942 ..	109	—	4·4	9·5
June, 1942 ..	153	7·5	6·2	9·8
Aug., 1942 ..	129	—	4·8	9·8
Nov., 1942 ..	160	—	—	—
Dec., 1942 ..	270	3·2	—	—
Feb., 1943 ..	192	3·4	5·2	9·2
Nov., 1943 ..	189	—	5·7	8·5

Blood phosphatase activity normal.

Plasma proteins normal.

CO_2 combining capacity of plasma 30·9 c.c.

Urea concentration test (April, 1942) 10 gm. urea given.

Before urea	0·3 per cent.
1 hr. after urea	0·4 ,, ,,
2 hr. after urea	0·4 ,, ,,
3 hr. after urea	0·5 ,, ,,

Daily blood sugars while in hospital were within normal limits.

Renal threshold for glucose = approx. 250 mgm. per cent. glucose.

INSULIN SENSITIVITY: 20·4 gm. glucose by mouth; 3·4 units soluble insulin i.v.

Fasting blood sugar ..	93 mgm. per cent.
10 min. after injection ..	94 ,, ,, ,,
20 min. after injection ..	87 ,, ,, ,,
30 min. after injection ..	86 ,, ,, ,,
45 min. after injection ..	93 ,, ,, ,,
60 min. after injection ..	100 ,, ,, ,,

TABLE 1—GLUCOSE TOLERANCE TESTS
(mgm. glucose per 100 c.c. of blood)

DATE	Feb. 3, 1942		Feb. 30, 1942		Mar. 19, 1942		June 17, 1942		July 23, 1942		Nov. 24, 1942		Nov. 10, 1943	
DOSE	20 gm.		50 gm.		20 gm.		20 gm.		50 gm.		50 gm.		50 gm.	
		Urine sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar
Fasting blood sugar ..	104	0	92	0	78	0	91	0	88	0	71	0	99	0
Glucose given														
½ hr. after	134	0	152	0	134	0	—	0	159	0	105	0	192	0
1 hr. after	202	0	243	0	174	0	169	0	207	0	158	0	309	Trace
1½ hr. after	258	0	239	Trace	179	0	115	0	293	Trace	221	0	378	+
2 hr. after	298	0	201	Trace	127	0	115	0	305	+	278	+	384	+
2½ hr. after	174	0	205	0	106	0	70	0	286	+	337	+	378	+

Case 2. Female, aged 3 years when first seen. Her mother noted the thirst when the patient was just over twelve months old. When first examined (Dec., 1941) she was a backward child. Her height was 31 inches, and weight 23 lb. The trunk–limb ratio normal. Her blood pressure was 105/70 mm. Hg. The clinical examination was negative. Her urine was pale, specific gravity 1002–1016, and contained no abnormal constituents. The x-ray of the skull was normal. No radiological evidence of rickets noted. A plain renal x-ray showed no opaque shadows; kidney shadows not outlined. On normal diet the blood sugar reached its maximum half an hour after mid-day (200 to 230 mgm. per cent. of glucose). No sugar was found in urine after blood specimens taken. Daily urine tests over a period of three months and during several short subsequent periods showed no albumin apart from a trace on one occasion. The case was last reviewed in November, 1943. Her height was 34½ inches and weight 29½ lb. Her blood pressure was 110/70 mm. Hg. The urine contained no albumin. No radiological evidence of rickets traced.

BLOOD CHEMISTRY
(mgm. per 100 c.c.)

Date	Blood urea	Blood creatinin	Serum calcium	Serum phosphorus
Jan., 1942 ..	27	—	—	—
Dec., 1942 ..	72	1·5	11·5	4·7
May, 1943 ..	44	—	—	—
Nov., 1943 ..	35	—	11·3	3·6

Blood phosphatase activity normal.

Urea concentration test (Dec., 1942) 4 gm. urea given.

Before urea	0·7 per cent.
1 hr. after urea	0·9 ,, ,,
2 hr. after urea	0·5 ,, ,,
3 hr. after urea	0·9 ,, ,,

Urea clearance = 52 per cent. average normal function (blood urea = 71 mgm. per cent.).

Creatinine clearance, filtration per minute = 78 c.c.

Insulin sensitivity = normal.

Renal threshold for glucose = approx. 250 mgm. glucose. See table 2 for glucose tolerance.

Case 3. Male, aged 7 years. Thirst was first noted when he was twelve months old. He was never very active. Generalized oedema gradually developed in October, 1942. He was treated at another hospital for nephritis and bronchitis for three months during which period the oedema gradually subsided. Thirst and polyuria had been marked since. When first examined (July, 1943) he was a spare, intelligent boy, with sallow skin. His height was 41 inches, weight 34 lb. Trunk–limb ratio was normal. His blood pressure was 112/70 mm. Hg. Clinical examination was negative apart from evidence of bronchitis. His urine was pale, specific gravity 1008 to 1016, and twenty-four-hour volume 14 to 41 oz. Albumin (++) was found. The centrifuged deposit showed 8 red blood cells per field, with occasional pus cells, and a few granular casts. An excretion urogram (12 c.c. uropac) showed no dye in pelves, ureters or bladder. The kidney shadows were small in size. Daily blood sugars half an hour after lunch ranged from 204 to 262 mgm. per cent.

BLOOD CHEMISTRY
(mgm. per cent.)

Date	Blood urea	Blood creatinin	Serum calcium	Serum phosphorus
July, 1943 ..	165	4·8	9·3	8·9

Urea clearance = 6·5 per cent. average normal function. (Blood urea 219 mgm. per cent.)

Plasma proteins 6·2 gm. per cent.

GLUCOSE TOLERANCE TEST
Date: July, 1943

Dose	50 gm.	
		Urine Sugar
Fasting blood sugar ..	69	0
½ hr. after glucose ..	153	0
1 hr. after glucose ..	161	0
1½ hr. after glucose ..	193	0
2 hr. after glucose ..	220	0
2½ hr. after glucose ..	261	Trace

Renal threshold for glucose = approx. 250 mgm. glucose.

Case 4. Female, aged 17 months. She had always been a wet baby, passing urine every quarter hour. There was marked nocturnal enuresis. She drank two pints of cow's milk daily and four cups of tea. On examination her height was 27 inches, weight 14 lb. 8 oz. She was able to toddle. The limb–trunk ratio was normal. Clinical examination was negative. Her urine was pale, with a trace of albumin but no other abnormal constituents. There was no radiological evidence of rickets or other bone

TABLE 2—GLUCOSE TOLERANCE TESTS (Case 2)
(mgm. glucose per 100 c.c. of blood)

DATE	Jan., 1942		Dec. 11, 1942		Dec. 22, 1942		Jan., 1943		May, 1943		Nov., 1943	
DOSE	14 gm.		40 gm.		60 gm.		50 gm.		50 gm.		50 gm.	
		Urine sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar		*Urine* sugar
Fasting blood sugar ..	84	0	71	0	—	0	73	0	86	0	84	0
Glucose given												
½ hr. after	121	0	139	0	243	0	172	0	—	0	209	0
1 hr. after	108	0	150	0	300 (child vomited)	0	224	0	213	0	375	0
1½ hr. after	91	0	164	0	224	0	251	Trace	157	0	175	0
2 hr. after	87	0	187	0	132	Trace	197	0	139	0	139	0
2½ hr. after	—	—	164	0	—	—	143	0	90	0	139	0

FIG. 1

abnormalities. While in hospital the child drank large quantities of fluid and passed much urine, but it was impossible to estimate even approximately the twenty-four-hour volume. This child has a twin brother who is healthy and normal in every respect (fig. 1).

BLOOD CHEMISTRY

(mgm. per cent.)

Date	Blood urea	Serum calcium	Serum phosphorus
February, 1944	104	13·5	5·3

Blood phosphatase activity slightly raised.
Plasma proteins 6·3 gm. per cent.

GLUCOSE TOLERANCE TESTS

DATE	Feb. 15, 1944	Mar. 2, 1944
DOSE	11 gm.	20 gm.
Fasting blood sugar ..	91	—
½ hr. after glucose ..	128	110
1 hr. after glucose ..	142	135
1½ hr. after glucose ..	117	107
2 hr. after glucose ..	75	—
2½ hr. after glucose ..	71	—

Discussion

The purpose of this article is not to discuss the theories of pathogenesis of renal dwarfism but simply to record the changes in carbohydrate metabolism which have been observed in three of the four cases studied. These cases show a raised renal threshold for sugar (approximately 250 mgm. per cent. glucose) and a variable degree of diminished carbohydrate tolerance. From the data available it has not been possible to draw any conclusions regarding the causation of these changes. It is of interest, however, to recall that Lander et al. (1925) obtained similar glucose curves and a raised renal threshold for glucose in adolescents and adults suffering from nephrosclerosis with little or no renal insufficiency and that Castaigne and Chaumerliac (1939) found that a high renal threshold for glucose is very common in chronic sclerosing nephritis.

Hagedorn and Jensen method was used for all blood sugar estimations. (Capillary blood specimens were taken.)

Thanks are due to Dr. H. T. Ashby for allowing the publication of case 2 and to Dr. M. Flowerday for her assistance with the first two cases.

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CASE REPORTS

CONGENITAL HEMI-ATROPHY

BY

LILLY H. ZONDEK, M.D.

Not much detailed information is available as to the causes and origin of structural asymmetries. Congenital hemi-atrophy is a rare developmental abnormality in which parts or all of one side of body are of diminished size. As a rule all tissues are affected to a similar extent. The condition should not be confounded with the unilateral atrophy associated with motor disorders such as unilateral paralysis and unilateral athetosis.

In 1927, in a survey of world literature, starting from 1859, Kraus and Perkins found only eight cases of congenital hemi-atrophy in five of which the whole side of the body was affected. The other three were confined to the leg in two cases, and to the face and leg in one case. More cases have been reported since, and in 1939, in another survey of world literature, Landauer found twenty-two cases of congenital hemi-atrophy, eight of which only showed an affection of the whole side of the body.

Congenital hemi-hypertrophy is, in many ways, the counterpart to congenital hemi-atrophy. Although also a rare condition, more cases of hemi-hypertrophy have been reported than of hemi-atrophy. Both conditions are sometimes associated with retardation in mental development and with vasculo-cutaneous disturbances, but these are met with much less frequently in unilateral atrophy than in unilateral hypertrophy. Perhaps these two latter affections are not caused by two different agents, but by either hypo- or hyperfunction of the same agent respectively.

The mechanism which brings about preferential asymmetry seems to act during a comparatively early stage of embryonic life. Probably the agency responsible for developmental asymmetry must be looked for within the developing embryo, and not in conditions of the uterine environment, as so many different structures are affected.. Various authors assume that the central nervous system has a trophic function in development and that thus unequal differentiation of cerebral centres may modify growth asymmetrically. Kraus and Perkins hold the view that cerebral portions of the visceral nervous system exert a trophic control not only on glands and smooth muscle but also on striated muscle, tendons, bone, skin, hair, in short, on all tissues of the body. They assume that these centres are located in the hypothalamic region in or about the floor of the third ventricle, as well as in the cell groups lying about the tuber cinereum. Furthermore, it is now also generally believed that from cell groups in the posterior part of the hypothalamus a directing influence is exerted over the function and trophic activities of the sympathetic system. On the other hand, evidence has been obtained that dysfunction of the sympathetic can be the cause of unilateral atrophy. Cases of facial hemi-atrophy have been reported associated with changes in the sympathetic on the affected side.

From this point of view it may be of interest to discuss some conditions which are frequently associated with unilateral atrophy. There are, to begin with, two clinical conditions in which hemi-atrophy is frequently met with, chondrodysplasia (Ollier's disease) and scleroderma. With regard to both these affections theories have been brought forward which assume that dysfunction of the sympathetic plays an important part in their pathogenesis. Furthermore, various instances of progressive (non-congenital) facial hemi-atrophy have been reported which show a definite relation to changes in the sympathetic system on the affected side. There are, lastly, various instances of total or partial hemi-hypertrophy associated with vasculo-cutaneous abnormalities, and which have been attributed to unbalanced action of the sympathetic.

Of these conditions Ollier's disease will be more fully described here as the case reported below showed some bone changes similar to those seen in chondrodysplasia.

Chondrodysplasia (Ollier's disease)

Chondrodysplasia is an osseous dystrophy affecting the long bones and the metacarpophalangeal skeleton. In some cases the vertebral bodies have also been found to be affected. (The osseous changes can be demonstrated by skiagram.) It is an affection of growth with arrest of growing parts of the skeleton. Ollier (1899) emphasized as an outstanding clinical character of the disease an asymmetrical involvement of the body, a ' one-sidedness.' One of the essential features of the disease is the retardation of growth of one or both limbs on the affected side, sometimes associated with compensatory scoliosis. The term ' Ollier's disease ' has now been confined by a number of authors to those cases of osseous dystrophy which show an asymmetrical involvement of the body as an outstanding clinical feature.

Chondrodysplasia usually starts in early life. Cleveland (1928) describes a case in which the first signs of asymmetry were noticed at the age of six months, so perhaps the determining agent begins to act during embryonic life. The affection is progressive for several years but later on tends to heal spontaneously, and in the later years of childhood the limbs on the affected side grow at the same rate as the limbs on the sound side.

Nothing definite is yet known as to the pathogenesis of chondrodysplasia. Bentzon (1924) holds the view that Ollier's disease represents the typical reaction of the bone to certain disorders in the innervation of their blood-vessels. He also stresses the fact that the affection is often confined to one half of the body. From an experimental standpoint, working with rabbits, he was able, by interrupting the sympathetic nerves to produce in several instances structural changes similar to those seen in Ollier's disease. Murk Jansen (1928) believes that chondrodysplasia is the result of a retardation of the differentiation of cartilage cells consequent upon a deficient blood-supply which may be due to vasoconstriction from faulty action of the sympathetic nerves. It may thus be concluded that, perhaps, sympathetic dysfunction plays an important part on the pathogenesis of Ollier's disease.

Scleroderma

Scleroderma is now considered by many authors to be an angiotrophoneurosis in which unilateral atrophy frequently develops as a secondary symptom. If the disease starts during youth, the growth of limbs on the affected side may suffer.

Cockayne (1916) found several instances of complete hemi-atrophy (non-congenital) with scleroderma of the atrophic parts of the body. Meyer (1936) assumes that the common cause for hemiatrophy and scleroderma may be looked for in an abnormal function of the sympathetic system, which reacts in some instances by causing scleroderma, in others by causing a hemi-atrophy or a combination of both abnormalities according to the part of the sympathetic which is particularly affected.

Facial hemiatrophy

In 1846 Romberg described a case with wasting of one side of the face. He called this affection 'facial hemi-atrophy' as a proof for the existence of trophic nerves.

Jendrassik (1884) assumes that the cause of facial hemi-atrophy is a lesion of the sympathetic cervical ganglia or of the fibres of Remak connected therewith, whereas Archambault and Fromm (1932) are of the opinion that sympathetic implication is its only underlying cause. This view has been confirmed by clinical observations. Brüning and Kroll (Meyer, 1936) found alterations in the ganglion cervicale superior in some instances of facial hemi-atrophy. Manthey (1928) reported a case of facial hemiatrophy developing after cut-injury of the cervical sympathetic and in a case reported by Bost (1927) the cervical sympathetic had been injured by fracture of the clavicle.

Although in all these instances the hemi-atrophy is affecting the face only, and is mostly of a non-congenital type, they may furnish a proof for the essential part which the sympathetic system plays in the pathogenesis of unilateral atrophy. The condition is strictly unilateral. It extends gradually, involving skin, fat and subcutaneous tissues until the entire side of face is affected. The bones show retarded growth or atrophy.

Hemi-hypertrophy and vasculo-cutaneous disturbances

Congenital hemi-hypertrophy is frequently associated with vasculo-cutaneous disturbances, e.g. pigmentation or haemangioma. Furthermore, diffuse angioma are often accompanied by local gigantism or partial hemi-hypertrophy. It has been assumed that this unilateral overgrowth might be the result of an unbalanced action of the sympathetic system, giving rise to an inequality in blood flow or distribution.

Report of case

J.E. a boy, aged 11 years, was admitted to the Queen Elizabeth Hospital for Children, Bayford, Herts., in January 1944.

Family history: The patient's mother is healthy, but 'highly strung.' The patient's father, who deserted the mother soon after the child's birth, is said to have been healthy and nothing abnormal has been reported in his family. No physical or mental abnormality can be determined in the mother's family.

Patient's history: The patient, an only child, was a full-term infant. His was an instrumental delivery. Birth-weight was 5 lb. 6 oz. He was bottle-fed. No definite date is available as to the starting of dentition, but he is said to have acquired his teeth rather early. He sat up when ten months' old, began to talk at fourteen months and started walking with support of a specially constructed orthopaedic boot at the age of two years. He has had measles, rubella, mumps, whooping-cough and chicken-pox.

At birth the child presented a marked underdevelopment of the right side of the body. The right side of the face was much smaller and flatter than the left one, the right arm and leg showed a remarkable shortening, he had a dorsal scoliosis to the right and a kyphosis. Testicles were absent from scrotum. During the first year of life the atrophy of the right side of the face became gradually less marked. During the following years, according to his mother's statement, this did not increase to any remarkable degree, the rate of growth of both apparently almost keeping pace with each other. The kyphoscoliosis, however, became much more conspicuous. He was treated in various hospitals where he received all sorts of endocrine therapy (elityran, ant. lobe pituitary hormone), as well as osteopathic treatment, but with no success. He could move all limbs well and never showed any paralysis. Mentally he was bright and intelligent and went to a normal school until September 1943, where he was backward in physical attributes but appeared mentally alert. Since then he has been taught at home.

Examination: The patient is a small boy, his height corresponding to that of a child aged five

years. The most marked deformity, at first sight, is the conspicuous kyphoscoliosis. The face is somewhat asymmetrical, and the right arm and leg are shorter and thinner than the left ones. He walks with a limp, owing to the shortening of the right leg.

HEAD: The head is of normal shape. The face shows some degree of asymmetry, the right side being somewhat flatter and smaller than the left.

CRANIAL NERVES:

1st to 10th: Normal.

11th nerve: Function of both sternomastoid and trapezii muscles somewhat restricted, but this is probably mostly due to the deformity and fixation of the spine which does not allow free movements.

12th nerve: Tongue protrudes in midline. No fibrillation.

TEETH: The teeth are sound, but rather crowded together and in bad position.

THROAT: Normal.

NECK: The neck is short, owing to the deviation to the left of the cervical spine. Movements restricted.

THORAX: The thorax is grossly deformed. The shoulders are kept high, the right one slightly higher than the left one. The upper thoracic spine shows considerable lateral deviation with the convexity to the right, the cervical and the lower thoracic spine show a compensatory scoliosis with the convexity to the left. There is a conspicuous kyphosis of the dorsal spine. The sternum protrudes considerably, thus causing a vaulted appearance of the anterior wall of the chest. The inferior angle of the right scapula is somewhat higher and farther from the middle line than that of the left scapula.

HEART: The heart is displaced upwards and outwards. The dullness extends over an almost quadrangular area, the lower border running in the third intercostal space from the left sternal border to just outside the midclavicular line, the upward border running almost parallel in the first intercostal space. The apex beat is palpable in the third intercostal space, $\frac{1}{3}$ in. outside the midclavicular line. All sounds are normal. The pulse is normal in volume and rate. B.P. 95/60 mm. Hg.

RESPIRATORY SYSTEM: The percussion note over the right side of the chest is hyperresonant, more so anteriorly than posteriorly. The percussion note is normal over the left lung. Breath sounds are feeble, especially posteriorly, but everywhere there is normal vesicular breathing. Respiration rate is normal.

ABDOMEN: The abdomen is flat. Muscular development fairly good. Liver and spleen not palpable. Abdominal reflexes present and equal. Both testes are absent from the scrotum and cannot be felt in the inguinal canal. No hernia.

EXTREMITIES:

Arms: Left arm normal.

Right arm: The right arm is shorter ($2\frac{1}{2}$ in.) and thinner than the left. The palm and thenar eminence are flattened. The middle phalanx of the ring finger shows a slight lateral abduction, whereas the distal phalanx is kept in a slightly flexed position. The little finger is small and shows a marked contraction, with palmar flexion in both phalangeal joints, and slight dorsal flexion and ulnar abduction in the metacarpo-phalangeal joint. All movements with the exception of the ring- and little finger, are normal and not restricted, but there is some degree of decreased muscular power as compared with the left arm.

There exists some laxity of the elbow joint and, especially, of the metacarpo-phalangeal joint of the thumb, thus allowing hyperextension. All reflexes are normal and equal on both sides. The patient is left-handed.

LEGS:

Left leg: Normal.

Right leg: The right leg is shorter ($2\frac{3}{4}$ in.) and thinner than the left one. All movements are normal and not restricted, but the muscular power is somewhat decreased in comparison to the left leg. All normal reflexes present and equal. No abnormal reflexes.

There is no evidence of ataxia or dysergia. No tremors, twitchings, choreiform movements or muscular spasms are present. All tests for touch, pain, temperature, vibratory, muscle, bone and tendon sense elicit normal and accurate responses.

THE SPEECH is normal.

THE SKIN is smooth, of normal consistency and there is no hyperhidrosis. The scalp hair is dense and equally distributed.

SLEEP: Normal.

APPETITE: Normal. Patient does not suffer from abnormal thirst.

MICTURITION AND BOWEL ACTION: Normal.

MENTAL CONDITION: The patient is of average intelligence. He is bright and alert, but rather unstable emotionally and will break into tears on the slightest provocation. He is noisy, over-talkative and boisterous and tries to attract attention by every conceivable means. When together with other children he adopts a domineering and provoking, at times even aggressive attitude. He is witty, although in a somewhat affected manner. He draws extremely well. He gets on well with younger children, who admire him because of his witticisms and among whom he quickly makes himself the centre of attention, but he has difficulties in adjusting himself to the company of children of his own age group who are inclined to resent his boastful, provoking behaviour and, in their turn, deride him because of his physical deformity.

X-ray examination:

SKULL: There is a slight flattening of the right side of the skull. Otherwise the skull is normal. Pituitary fossa normal (fig. 1).

THORAX: There is a gross deformity of the upper dorsal spine and upper right ribs, with marked kyphoscoliosis convex to the right with a wedge-shaped deformity of the vertebral bodies. There is some degree of compensatory scoliosis convex to the left of the cervical and lower dorsal spine. The upper thoracic vertebral bodies show a deficiency in bone structure, with abnormal ossification, and contain irregular strands of calcareous material. Their cortex is thin and irregular, and there appears to exist some fusion between II and III, and IV, V, VI and VII. The right ribs are thin and atrophic, especially the upper six, and take a downward course, forming an acute angle with the vertebral bodies. The fourth to eighth left ribs are crowded

FIG. 1

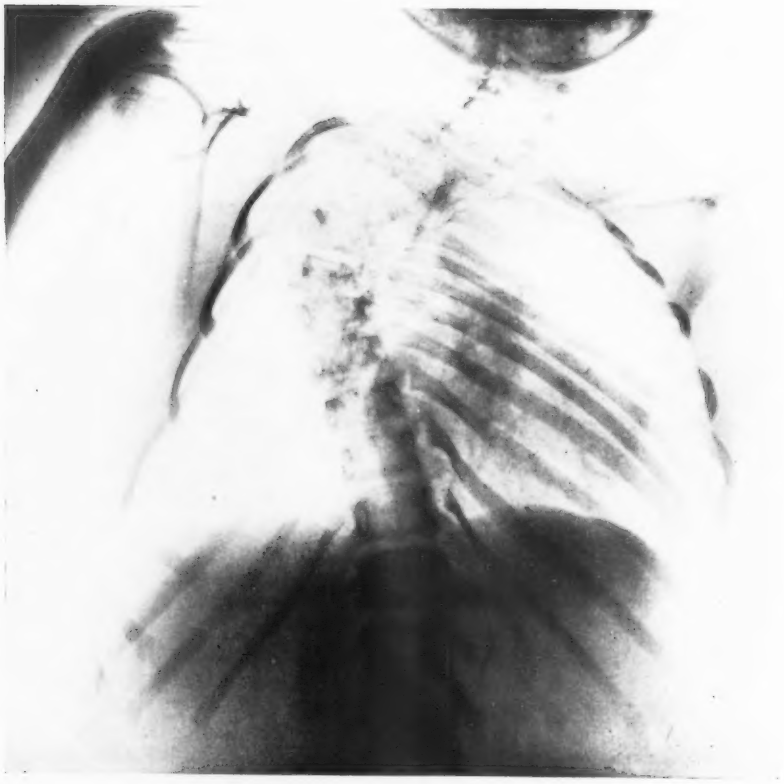

FIG. 2

together and their intercostal spaces are narrow (fig. 2–4).

The lumbar spine appears to be normal.

The right os ilium is smaller than the left one.

EXTREMITIES: All bones are slender. The bones on the right side, including the carpal and tarsal bones, are smaller and thinner than the left ones. There is some lateral abduction of the middle and distal phalanges of the right ring finger, and marked plantar flexion of the middle and distal phalanges of the right little finger, with abduction of the 1st phalanx. The middle and distal phalanges of this finger show a high degree of atrophy. Both feet are small, the right one smaller than the left one, but otherwise well developed. The bone structure is normal, the development is normal for the age and there is no delay in ossification (fig. 5–9).

FIG. 3

MEASUREMENTS (IN INCHES)

Length of body (standing on both legs, without correction of the shortening of the right leg)	42½
Normal length of a child 11 years old	54
Vertex to symphysis	21

	Right	Left
Symphysis to sole	21½	23½
Proc. zygomaticus to chin	3	3½

ARMS:	Right	Left
Length of whole arm	18½	21
Humeral-clavicular juncture to lateral condylus humeri	8	9
Lateral condylus humeri to styloid process of radius	6	7
Radio-carpal joint to tip of middle-finger	4½	5
Circumference upper arm	6¼	7
Circumference forearm	5	5½
LEGS:		
Total length of leg	21¼	24
Spina iliaca ant. sup. to medial malleolus	23½	25
Trochanter maj. femoris to lat. condyle of tibia	11	12
Lateral condyle of tibia to lat. malleolus	9¼	10½
Medial condyle of tibia to medial malleolus	9	10
Medial malleolus to top of big toe	4¼	5
Circumference thigh	10¾	12¼
Circumference lower leg	7¼	8½

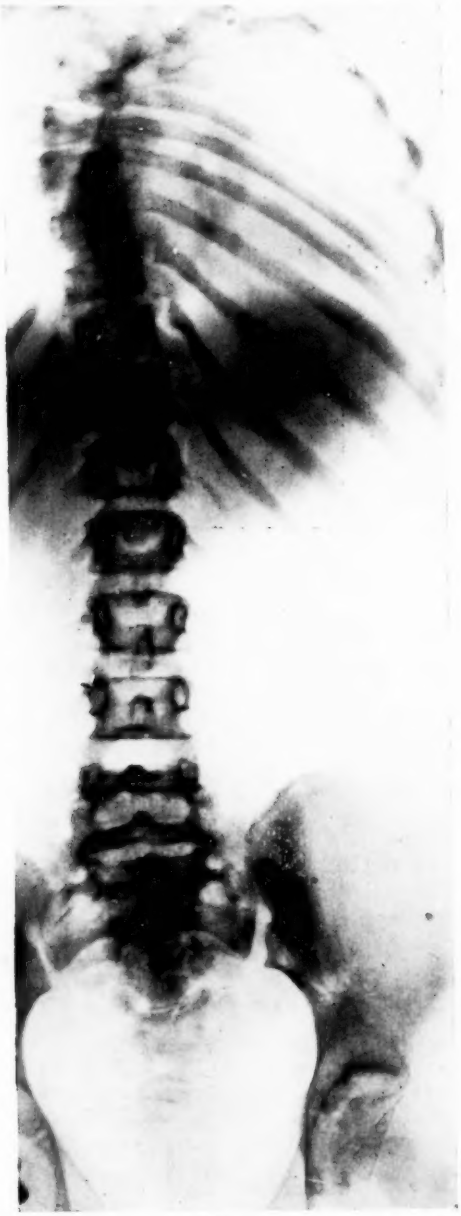

FIG. 4

FIG. 5

Laboratory examinations

URINE:

Specific gravity: 1023.
Deposit: Nothing abnormal detected.
Total output within 24 hours: 1280 c.c.

BLOOD:

Erythrocytes	4,560,000 per c.mm.
Haemoglobin	82 per cent.
Colour index	0·9
Leucocytes	8,600 per c.mm.
Polymorphonuclears	61 per cent.
Lymphocytes	32 per cent.
Mononuclears	6 per cent.
Eosinophils	1 per cent.
Basophils	0

SUGAR TOLERANCE:

	Blood sugar (mgm. per cent.)
0 hours (23 gm. dextrose by mouth)	97
½ hour	170
1 hour	131
1½ hours	103
2 hours	95

Summary and conclusion

The case under discussion is a total congenital hemi-atrophy in a boy aged eleven years, affecting the right side of the body, with a high degree of kyphoscoliosis. The body length corresponds to that of a child five years old, but this is probably due to the deformity of the spine. The extremities on the sound side are of about the normal length for a child aged eleven years. The long bones and the metacarpo-tarsal skeleton on the affected side are shorter and thinner than the ones on the sound side, but the bone structure, as seen by x-ray, is normal and there is no delay in ossification. The under-development is not confined to the bones alone, but also affects the soft tissues, as shown by the lesser circumference and the decreased muscular power of the limbs on the right side. The upper six right ribs show a high degree of atrophy. The vertebral bodies of the upper thoracic spine, especially II to VII, show gross deformity and abnormal structure of the bone tissue. Their appearance with the thin, irregular cortex, the deficiency of bone structure, with irregular strands of calcareous material, is similar to the changes seen in Ollier's disease. The extreme degree of wedge-shaped deformity is, of course, mostly due to the kyphoscoliosis which, in

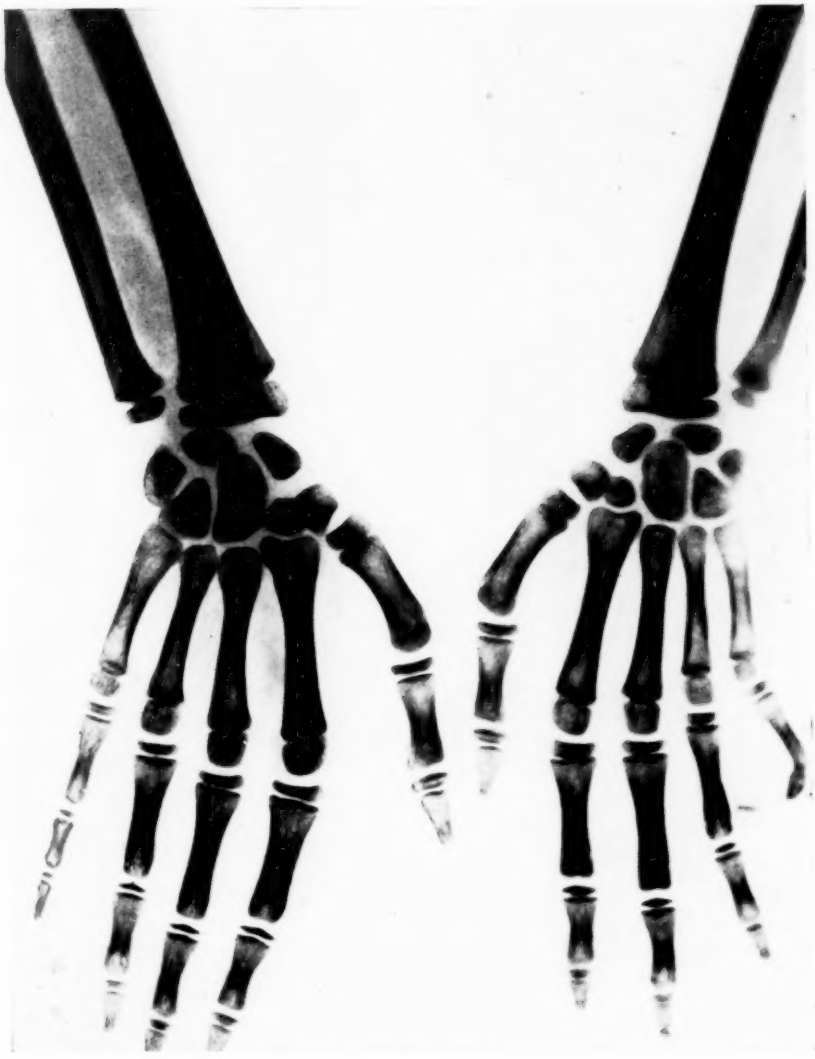

FIG. 6

its turn, is partly due to the postural disturbances exerted by the underdevelopment of the right side of the body. It is possible, however, that the soft consistency of these bones, caused by the osseous dystrophy, played a part in aggravating their deformity.

The patient showed two more abnormalities, the contracture of the right hand little finger and cryptorchidism. The contracture of the little finger, with fixed palmar flexion of the middle and distal phalanges and slight dorsiflexion of the proximal phalanx, and the slight palmar flexion of the middle and distal phalanges of the ring finger, lead to the suspicion that this is a congenital contracture of the affected fingers, which is a comparatively common inherited deformity. It has been suggested that this abnormality is probably due to imperfect development of the anterior ligament of the first interphalangeal joint. Regarding the cryptorchidism it cannot be determined here whether this condition is due to hormonal deficiency or to anatomical deficiency. The former is the more common cause of undescended testicles, but lately the fact has been stressed that anatomical defects appear to play an important part in many cases of cryptorchidism.

One further note may be made here about the patient's mental make-up. His very noisy, boastful, provoking and, at times, aggressive behaviour can be explained as a defence mechanism. By overstressing his mental capacities he tried, unconsciously, to counteract the feeling of inferiority caused by his physical deformity. He thus 'overcompensated his inferiority-complex.' As a consequence, his social adjustment with children of his own age-group was rendered rather difficult.

Nothing definite can be said regarding the pathogenesis of this case. The factor determining the underdevelopment of the right side must have acted during embryonic life as the hemi-atrophy was found to be present at birth. Furthermore, the action of this agent was probably mostly confined to the period of intrauterine development, as the discrepancy in length between the two sides of the body is said not to have much increased after birth.

An influence by the pituitary gland cannot be excluded. But one of the main features of hypo-

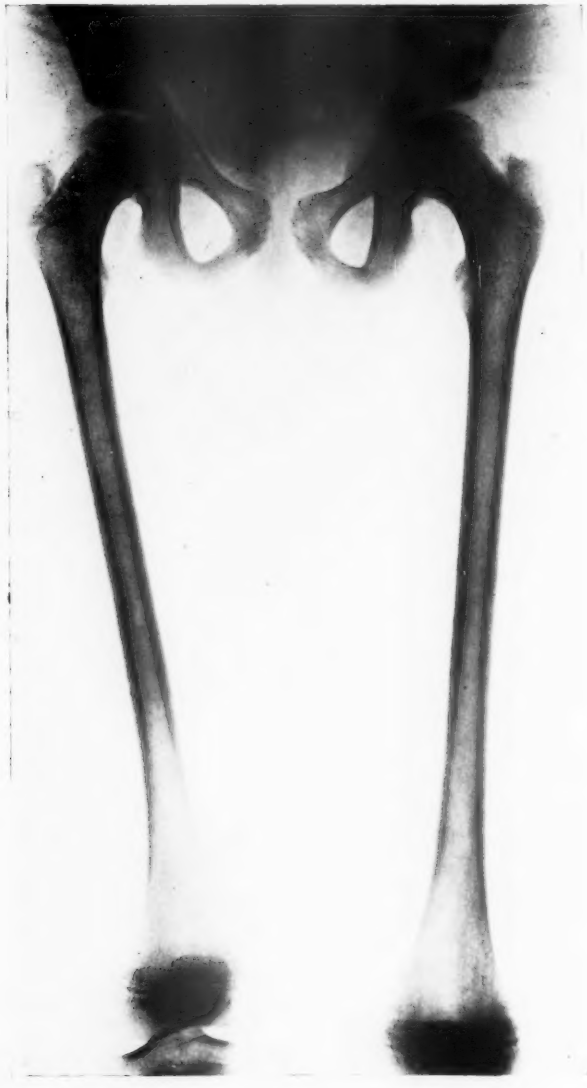

FIG. 7

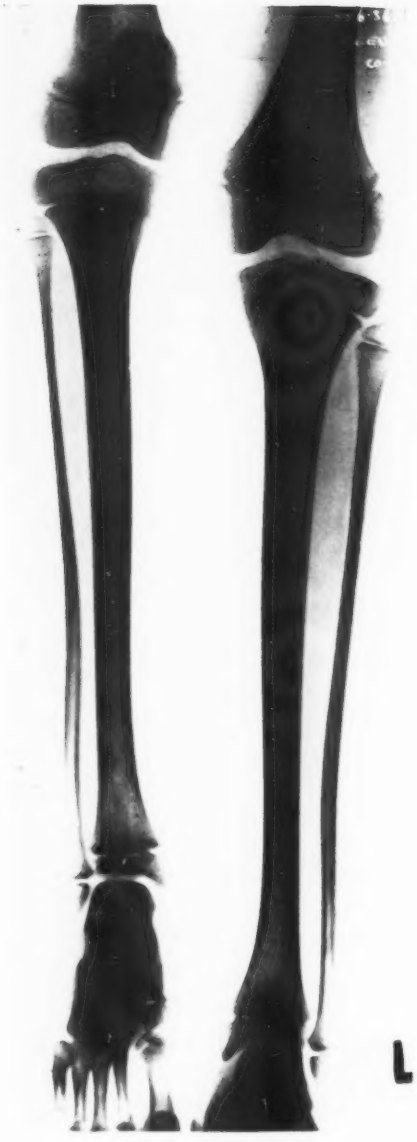

FIG. 8

physeal dwarfism is unimpaired symmetry of the body. The cryptorchidism in this case may be a symptom of hypopituitarism, but, on the other hand, the incidence of this abnormality is high and it cannot therefore be concluded, from this fact alone, that the hemi-atrophy is due to hypophyseal deficiency, i.e. lack in growth hormone. Besides, that would not explain the unilaterality of the affection.

It has been suggested that cerebral portions of the visceral nervous system exert a trophic control on all body tissues, perhaps partly via the sympathetic system, and may thus influence growth asymmetrically. It has also been shown that facial hemi-atrophy may be brought about by changes or injury of the sympathetic on the affected side. It has further been mentioned that scleroderma which is frequently associated with hemi-atrophy as a secondary symptom, may have its origin in an abnormal function of the sympathetic system. Lastly it has been pointed out that sympathetic imbalance may play a major part in the pathogenesis of chondrodysplasia, in which a unilateral arrest of growth is frequently met with. From that point of view one further note may be made regarding the relations existing between congenital hemi-atrophy and Ollier's disease. In both affections the responsible agent acts during early life. Hemi-atrophy is congenital (as in the reported case). Ollier's disease starts in infancy or early youth (the case reported by Cleveland showed the first symptoms at six months), i.e. it may already be present at birth. Both conditions are not progressive during the whole time of adolescence. In the reported case of hemi-atrophy the growth of both sides apparently almost kept pace with each other after birth. Ollier's disease usually comes to a standstill in the later years of growth. Ollier's disease is frequently (according to several authors always), confined to one side of the body and the

FIG. 9

affected limbs show an arrest in development. Both unilaterality and underdevelopment are the main features of hemi-atrophy. Furthermore the reported case showed changes in several vertebral bodies similar to those seen in Ollier's disease. It thus appears that some relationship might exist between these two abnormalities.

A final conclusion regarding the etiology of congenital hemi-atrophy can, however, not be given, as some still unknown morphogenetic factor is probably concerned.

Thanks are due to Mr. H. W. S. Wright, Hon. Surgeon to the Queen Elizabeth Hospital for Children, Bayford, Herts., for the opportunity to examine this case and for his permission to publish it, and to Sir John Fraser, Royal Infirmary, Edinburgh, for his kind help and assistance.

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PAROXYSMAL TACHYCARDIA IN INFANCY

BY

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The occurrence of paroxysmal tachycardia in childhood has been noted in case reports for over twenty years. Cases were reported in the English press in 1924 and 1925, but after this interest seems to have lapsed until 1941 when a review of the subject, with special reference to infancy, was made by Hubbard (1941) with a report of nine cases. Full references to the literature up to that year are to be found in his paper and in a paper by Hobbs (1941) reporting another case. Subsequently case reports have been published by Blackford and Hoppe (1943) and by Hubbard and Starback (1943).

Hubbard differentiates cases in infancy from those in older children, because of what he believes to be a characteristic syndrome in young infants, consisting of fever, leucocytosis, dyspnoea, pallor, vomiting, and dilated heart with signs of congestive failure. Those of his cases which were cardiographed showed either auricular or nodal tachycardia, with ventricular rates varying from 220 to 305, but his 1943 case had a ventricular rate of 350. Although he believes the condition to be more common than has been recognized, it is sufficiently rare for it to be unusual for clinicians with many years of practical experience in children's work to have observed a case.

Clinical record

A girl baby born on August 13, 1944, the fifth child of apparently healthy parents, was admitted to the Royal Northern Infirmary on October 12, 1944. The pregnancy was full term and the mother was healthy throughout. The first child, born in 1939, a boy, is healthy. The second died in hospital in Dublin ' of a heart attack ' at the age of six weeks. It has unfortunately not been possible to trace the records of this child. The third, born in 1941, a girl, is healthy. The fourth child, a boy, now aged 1½ years, had been admitted to the Royal Northern Infirmary for a few weeks in August, 1944, for observation. There had been feeding difficulties with this boy (D.O'R.) when he was a few weeks old, which had necessitated his admission to hospital in Ireland. Subsequently he made excellent progress, and weighed 22 lb. at ten months when he had also learned to stand up, when he began to vomit and in a few weeks had lost 4 or 5 lb. in weight. He was reported as peculiar in behaviour, burying his face in the pillow, very fretful, and reluctant to feed. This state continued until he was examined at hospital on August 8, 1944, aged thirteen months. He was apathetic, hypotonic and disliked being handled. There were no signs of meningitis, nor any focal central nervous system signs. Tendon jerks were present: there was no photophobia, and no rash except on the buttocks. He was afebrile. His heart rate was 140–160 at this examination, but subsequently in the ward 100–120. Blood pressure 75/50. Blood sedimentation rate (capillary method) 13 millimetres at one hour. R.B.C. 4·79 million per c.mm., Hb. 85 per cent., W.B.C. 6,000 per c.mm. He gained weight, was trained to a mixed diet, resumed his progress and a tentative diagnosis of neurosis was made. He was readmitted after the death of his infant sister because of a recurrence of symptoms on November 14, 1944, aged eighteen months, weighing 20 lb. No fresh signs were discovered. His mother described his behaviour as suggesting an aversion to her.

Two children born to the father's brother are reported to have died rather suddenly in infancy.

The baby who is the subject of this case record was bottle fed and made steady progress until October 10, 1944, when she was discovered by her mother in her cot looking ' suffocated.' She was red in the face, sweating and gasping for breath. This condition obtained for about two hours when she improved, was given a feed and vomited. Subsequently she appeared to have spasms of pain, turning her head from side to side and pulling up her legs. She was restless all night and the following day breathing was laboured; she was fretful, was reluctant to take feeds, and vomited several times. The stools, which had previously been normal, now appeared to be undigested, and an umbilical hernia not previously noticed became evident when she was crying.

Examination. Shortly after admission the following note was made of her condition. General state of nutrition good. Eyes are sunken. Slightly cyanosed. Fontanelle normal. Respiration quick but not distressed. Temperature 105° F. Respirations 38. No physical signs of pneumonia. Buttocks raw. Offensive intestinal gas and undigested stool. Heart rate 240 with regular rhythm. No extrasystoles and no murmurs. General muscle tone normal. No head retraction nor other evidence of focal disease in nervous system. Total white cell count 20,000 per c.mm. The cardiogram (fig. 1) showed auricular tachycardia, rate 240, with right axis deviation. The heart rate was not

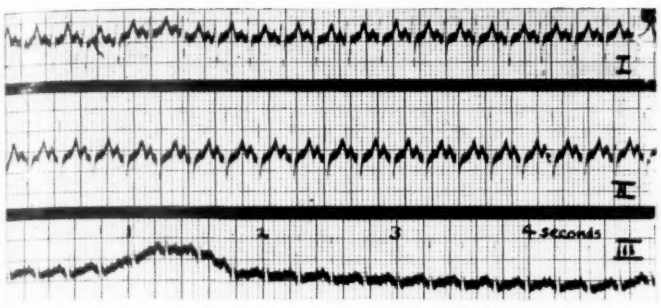

FIG. 1

influenced by compression of carotid or eyeball, or by alterations of posture.

The question of digitalis or quinidine therapy was debated, but it was decided to withhold both overnight until further experience of the child's condition had been gained, since there were no present signs of congestive failure. Three grains of chloral hydrate were prescribed followed by 1 grain every four hours and, because of the evidence suggesting an acute infection, sulphadiazine 0·5 gm. followed by 0·25 gm. every four hours.

On October 13, 1944, the infant appeared much better, was ready to take feeds (saline with corn syrup only), did not vomit, and the heart rate was slower. This improvement continued until the evening of October 14, 1944, the heart rate then being 160, when without any resumption of the tachycardia, a deterioration in the baby's condition set in. Feeds were again refused, and the infant appeared hypersensitive, starting at the slightest noise, and appearing distressed when touched or disturbed in any way. Head retraction with a tendency to opisthotonos appeared and intermittent squint. The spinal fluid by lumbar puncture was diffusely blood-stained and from cisternal puncture likewise. There was no excess of white cells: the Wassermann reaction was negative. The general condition now rapidly deteriorated, and the baby died.

Post-mortem examination. The autopsy showed an apparently normal heart, with no enlargement or signs of infection. No evidence of congestive failure in liver, spleen, kidneys or lung. There was slight atelectasis of the right lower lobe (an area which had been questioned on clinical examination as showing early signs of bronchopneumonia). Brain and meninges were apparently normal. There was no evidence of scurvy or rickets. The general report on the post-mortem examination was (Dr. A. Dick) —— 'Nothing from the post-mortem examination to account for the tachycardia. No evidence of any infective process or encephalitis found.'

HISTOLOGICAL EXAMINATION (Dr. H. J. Kirkpatrick). Heart (tissue from neighbourhood of interventricular septum). There is cloudy swelling and oedema. Congestion of vessels, but no inflammatory infiltration.

Brain. Vessels are congested and there is some oedema. In one or two places there is a little capillary extravasation of blood—probably not significant. No evidence of inflammatory process.

Comment

This infant did not have the signs of heart failure either in life or at the autopsy, nor did the mode of death suggest that the heart was the organ the function of which primarily failed. On the contrary, the whole syndrome in its latest stages was one of an acute encephalopathy. Hubbard suggests that the leucocytosis and fever in his cases were to be explained not on a toxic or infective basis, but as a direct result of heart failure and due to congestion of the lungs. It is impossible to accept such an explanation in this case. It is noteworthy that in one of his subjects, aged two weeks, the spinal fluid was examined and found to be xanthochromic and to contain red cells; this infant was readmitted to hospital at the age of four weeks with a recurrence of tachycardia, and again found to have a blood-stained spinal fluid. That this was not the only patient in whom symptoms suggestive of encephalopathy occurred, is shown by the fact that in another case meningitis had been diagnosed by the practitioner before admission to hospital, the baby being described as 'comatose.' It is, of course, possible that the haemorrhage into the spinal fluid in both Hubbard's case and the present one was traumatic, but it seems unlikely. The experienced operator recognizes fairly easily the difference between the haemorrhagic fluid which is the result of a disease process and one which has been caused by himself. In the present case, the blood cells were uniformly mixed with fluid which appeared haemorrhagic from the first, and cisternal puncture was done immediately, the child's head being a little raised throughout, the appearance of the fluid from the cistern being exactly the same as that obtained from the lumbar region. In Hubbard's case the spinal fluid was haemorrhagic on both occasions and was xanthochromic on the first occasion. The post-mortem appearances failed to disclose any gross meningeal haemorrhage, and it must be assumed that the blood cells had reached the spinal fluid by process of diapedesis. In so far as any positive conclusions could be drawn from the post-mortem examination, the picture resembled one of a toxic encephalopathy, not of any infective process.

In a paper entitled 'Human-Milk Intoxication,' Dr. Lydia Fehily (1944) describes a syndrome, often fatal in Chinese infants, which she considers due to intoxication by methylglyoxal and other products of incomplete carbohydrate metabolism in the breast milk of mothers suffering from beriberi.

> The acute syndrome she describes as one of 'vomiting, abdominal pain, diarrhoea, abdominal distension, stiffness of the neck and extremities, and convulsions. In the most acute form the attack consists of dyspnoea, cyanosis and running pulse. The attacks often end fatally, but in case of survival the infants pass into the chronic stage with symptoms of oedema, oliguria, aphonia, constipation, meteorism, neck retraction, enlargement of liver and right side of heart, loss of weight, retarded growth and marasmus.'

She suggests that the syndrome she describes is due to acute milk intoxication, but her reasons do

not amount to proof with any experimental work, e.g. the production of symptoms demonstrated by the giving of milk from a beriberi mother to the baby of an apparently healthy mother. She suggests that this syndrome is a possible explanation of cases of sudden dyspnoea and cyanosis, or of sudden death in breast-fed infants in the western hemisphere.

I have seen at least one attack of this kind in a breast-fed baby whose temperature reached 107° F., and in whom no definite physical signs were observed. This baby was already weaned when I saw it at the age of six days, but had been breast fed at the time that the attack occurred. There is, of course, no question of the whole series of cases of paroxysmal tachycardia which has been reported in the press from time to time and now numbers twenty or thirty, being accounted for by such an explanation as that offered by Fehily for her cases, nor does she specifically mention rapid heart rates as characteristic of the syndrome she is describing. The resemblance nevertheless between the two types of syndrome: (*a*) Dr. Fehily's infantile 'intoxication,' and (*b*) the syndrome of tachycardia with fever, leucocytosis, and symptoms suggestive of encephalopathy, is close enough to be worthy of remark.

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CONGENITAL MALFORMATION OF THE HEART IN ONE OF IDENTICAL TWINS

BY

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On June 12, 1944, Mrs. F. was delivered in her home of female twins. I had supervised her antenatally in this her second pregnancy, but the confinement was attended by the midwife only. There was a history of uniovular twins in both the patient's family and that of her husband. The pregnancy was normal except that at the third month she had a mild vaginal haemorrhage which was treated as a threatened abortion. Twins were suspected from this time owing to the size of the uterus, and confirmed later by x-ray examination. She became very distended in late pregnancy. The first stage of labour was long. The first child was delivered as an occipito posterior, weighing 5½ lb. The second child followed in five minutes and weighed 4½ lb. The single placenta followed; there was a small placenta succenturiata. The two cords were equal in size and attached to the main placenta.

The infants both appeared normal and breathed spontaneously, remaining a good colour. They were breast-fed six-hourly the first day for five minutes, four-hourly the second day, and three-hourly the third. Sterile water was given between feeds if required. Both sucked well at first, but at the end of the second day the smaller twin was noticed to be pale and she refused her feeds. The third morning she had two attacks of vomiting, with cyanosis of her lips only.

I saw her the third morning. Her breathing was shallow, with periods of apnoea. Her hands and feet were never cyanosed, her lips and face only at intervals. The chest moved poorly and breath sounds were almost entirely absent. The heart did not appear to be enlarged. There was a harsh systolic murmur over the base of the heart and tricuspid area. It was loudest in the second left interspace. The apical sounds were clear. The diagnosis of atelectasis with patent ductus arteriosus was made. The infant was given oxygen and two-hourly breast feeds from a pipette. She did not want her feeds and vomited some of them. The cyanotic attacks continued but were somewhat relieved by oxygen. She died early on the fourth day during an attack.

The first and larger twin seemed entirely normal in every respect. Recent x-ray examination including screening at four months of age shewed no radiographic abnormality.

Autopsy on the smaller twin showed almost complete atelectasis of both lungs. The heart was not enlarged, the pericardial sac and fluid were normal. The chambers and septa of the heart were normal. The ductus arteriosus was widely patent, being of the same calibre as the pulmonary artery. The aorta showed a marked constriction at the point of entry of the ductus arteriosus. Below this point it was of normal calibre. There were no other abnormalities.

Discussion

The rare occurrence of a congenital malformation in one of identical twins may throw light on pathological or physiological processes. I can find no other incidence of congenital defect in one of monovular twins, although occasionally abnormalities have been reported in both twins.

With regard to cardiac defects, Shirley Smith (1929) reported the occurrence of patent ductus arteriosus in both of monovular twins. Debreuil Chambarde (1927) reported transposition of the viscera in one of twins. Both had other abnormalities, one a mirror image of the other. Giustra (1939) found a case of cor biloculare in both twins.

According to Maude Abbott congenital cardiac abnormalities are generally due either to arrest of growth caused by disease in the foetal membranes, mother or germ plasm, or by disease in the foetus itself. Cardiac abnormalities are associated with other anomalies in 11 to 30 per cent. of cases. Rarely there is a family history of cardiac anomalies.

If the germ plasm itself is affected by any of these causes it is difficult to see how only one twin could be affected. The larger twin may have had the better nutrition throughout and the smaller twin suffered by an arrest of cardiac growth. The cords were both the same size, however, and the sizes of the twins were not grossly different. Regarding the other possibility of disease of the maternal tissue or foetal membranes, one of these may have been the cause in this case as shown by the vaginal haemorrhage in the third month. By that time the development of the heart is far advanced. Maude Abbott thinks that a patent ductus arteriosus may be caused by an acute infective process with primary involvement of the pulmonary trunk. It is often associated with other abnormalities, chiefly coarctation of the aorta. This represents an arrested foetal condition, possibly owing to a lowered state